A STUDY TO EVALUATE THE ASSOCIATION BETWEEN UROLITHIASIS AND METABOLIC SYNDROME

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I hereby declare that the thesis entitled "**A STUDY TO EVALUATE THE ASSOCIATION BETWEEN UROLITHIASIS AND METABOLIC SYNDROME**" submitted towards partial fulfillment of the requirements for the award of **MCh in Urology degree** to BFUHS is a compilation of original work carried out by me under the supervision of **Dr. Sandeep Sharma**, Professor & Head, Department of Urology, **Dr. Arvind Goyal**, Associate Professor, Department of Urology and **Dr. Naveen Mittal**, Professor & Head, Department of Endocrinology. No part of this thesis has formed the basis for the award of any degree previously.

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Dedicated

to

my Family,

friends

&

Teachers

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ABBREVIATIONS

BMI	Body Mass Index
BP	Blood Pressure
CVD	CardiovascularDisease
DBP	Diastolic Blood Pressure
FBS	Fasting Blood Sugar
HDL	High Density Lipoprotein
HTN	Hypertension
IDF	International Diabetes Federation
MetS	Metabolic Syndrome
NCCT KUB	Non contrast computed tomography kidney urinary bladder
NL	Nephrolithiasis
Non-MetS	Non-Metabolic Syndrome
SBP	Systolic blood pressure
T2DM	Type 2 Diabetes Mellitus
TG	Triglycerides
UA	Uric Acid
USG	Ultrasonography
WHO	World Health Organization

ABSTRACT

Introduction: Urinary stone disease is a common urological disease. Patients with metabolic syndrome have an increased risk of developing urolithiasis. This study assessed the association of metabolic syndrome and its components with urolithiasis in Indian patients.

Aim of Study: 1. To evaluate the relationship of Urolithiasis with metabolic syndrome constituents.

2. To evaluate the biochemical component of stone in metabolic syndrome.

Materials & Methods: The study was conducted among the patients admitted to Department of Urology, DMC&H, Ludhiana. The study design was a Cross-sectional study. Information was collected through a pre- designed Performa for each patient chosen to be a part of the study with preinformed consent. Analysis was done with the collected details.

Results: Total 180 patients with urolithiasis were divided into two groups (with [n = 21] and without metabolic syndrome [n = 159]). The mean age of total population was 46.27 ± 12.72 years with 129 males and 51 females. Mean BMI of MetS group and non-MetS group was 30.54 ± 1.97 and 23.97 ± 4.68 kg/m2 and were significantly different between both groups ($p < 0.05$). Proportion of patients and mean value of metabolic components which includes increased waist circumference, blood pressure, triglyceride, fasting blood sugar levels were significantly higher in patients with MetS and high-density lipoprotein levels was significantly reduced in metS group ($p < 0.05$). Patient with MetS were found to have increased risk of uric acid stones formation (44.44%).

Conclusion: This study indicates the presence of a significant association of MetS and its components with increased risk of urolithiasis and increased risk of uric acid stones in MetS patient.

Keywords: Metabolic syndrome, Risk, Urolithiasis, Uric acid, Obesity, IDF, FBS, HDL, TG, SBP, DBP, BMI, MetS

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INTRODUCTION

Urolithiasis is the most common and very painful disorder of urinary tract. Many people are suffering from urolithiasis problem all over the world [1]. Abo

ut 5–10% of the population in developed countries affects from stone formation in urinary tract, although it is very rare in some other countries. Urolithiasis is becoming a serious social problem due to its high incidence and recurrence rate [2].

Many reports have revealed that, during the past 25 years the frequency of kidney stone disease in developed societies has been increasing [3]. Until recently, the disease was mainly diagnosed in adulthood. At present, however, it more frequently affects children also, irrespective of their age. The prevalence of urolithiasis mainly depends on age, race, sex, socioeconomic factors, and place of residence (geographical region) [4]. According to the epidemiological data, in adults the prevalence of urolithiasis ranges from 1 to 20% [5, 6]. Highest incidence is noted between the age of 20 and 40 years [5]. Moreover, the prevalence varies across the regions of the world. In Asia, urolithiasis is diagnosed in 1–5% of the population. In Saudi Arabia, the prevalence of urolithiasis is the highest in the world and it is around 20.1%, Canada and United States; it is around 13–15%. The average prevalence noted in Europe is 5–9%. The difference in the prevalence rates within a single country may be due to the disease depends on a geographical region and historical period [7, 8]. Due to changes in socioeconomic conditions, lifestyle and better imaging, changes in the incidence and type of stones in terms of both site and the physical-chemical composition of stones has been observed [2].

Stone disease presents a complex model for interpreting the mechanisms involved in its genesis and development. Several genetic, nutritional, anatomic, and environmental factors along with the presence of concomitant diseases play an important role in the disease development [2]. The prevalence of urinary stones varies according to age. The prevalence is 10.58% in persons who are under 45 years of

age while in those over 65 it is 4.7% [9]. This correlation is probably due to the presence of conditions like obesity, hypertension, hyperuricemia, etc. Calculi in the urinary tract are more commonly observed in males than in females [4, 10]. It is observed that renal colic i.e., severe pain caused by a kidney stone, affects about 3-5% of women and 10-20% of men with a male-to-female ratio of 2.7:1. In India, 12% of the population is expected to suffer from urinary stones, out of which 50% may end up with loss of kidneys or renal damage [1]. Men have higher incidence than females are probably due to sex hormones [11]. The disease is more prevalent in the white race [4]. Some of the patients with urinary stones have a family history of stone disease, showing that it may be due to a polygenic defect with partial penetrance [9].

Temperature has an impact on kidney stones. According to research presented at the 103rd Annual Scientific Meeting of the American Urological Association (AUA), rising global temperatures could lead to an increase risk of kidney stones. Dehydration has been linked to stone disease, particularly in warmer climates [1]. Due to high temperatures perspiration insensibility increases which may further leads to more concentrated urine. This event promotes urinary crystallization and stone formation [9]. Diet may have a significant role on the incidence of urinary stones. The incidence has been steadily increasing, paralleling the rise in other diseases associated with the so called ‘Western diet’. Being obese (higher BMI) and increasing weight gain have been linked with high stone risk among men and women. In the development of urinary stones, diet and fluid intake may be important factors [1]. Greater risk of stone formation occurs in subjects with hypertension associated with excess body weight. Higher oxaluria and calciuria as well as supersaturation of uric acid and calcium oxalate seem to be the most important factors. Other important factors are Excess body weight, consumption of salt and animal proteins [12]. Postmenopausal women with low oestrogen levels and women who had oophorectomies removed have an increased risk for kidney stones [11]. Urolithiasis is a recurring disease. A recurrence is identified in 50% of patients within 5 years and in 80 – 90% of patients within 10 years. It is also identified in

obese children. The younger the child is at the time of diagnosis, the greater is the risk of recurrence, the more often the complications and also the treatment becomes difficult [4].

Metabolic syndrome is also known as “syndrome X” and “insulin resistance syndrome”. Metabolic syndrome consists of a group of disease states - glucose intolerance, dyslipidaemia, elevated blood pressure and central obesity. It is a fatal disease which is responsible for a threefold increase in the risk of atherosclerotic cardiovascular diseases (CVD) and increased mortality from CVD [13, 14]. Individuals with these characteristics commonly harbour a pro-inflammatory state, resulting in a pro-thrombotic condition [15]. Metabolic syndrome has become a major problem in public health. The prevalence in adults is around 20–25% throughout the world [16]. Over the past two decades, the number of people affecting with the metabolic syndrome have been increased worldwide. This increase is correlated with the global epidemic of diabetes and obesity [16, 17].

In obese population, all the components of metabolic syndrome are regularly detected. Assessment of the overall rise of type 2 diabetes, obesity, metabolic syndrome, and stone disease reveals potential connection between these conditions [13, 18]. Several studies demonstrated that increased BMI, weight gain and larger waist size connected with an increased risk of stone episodes [19]. Some of the components of metabolic syndrome have been related with the occurrence of nephrolithiasis (NL) or with biochemical abnormalities that in turn are linked to NL [15].The link between urolithiasis and metabolic syndrome has suggested a possible role of multiple metabolic risk factors in the development of urolithiasis[13,20]. The key parameters depicting metabolic syndrome include overweight, arterial hypertension and disturbances of the carbohydrate metabolism [15]. In metabolic syndrome, rise of uric acid stones, increase in urinary phosphate, and oxalate levels and an overall increase in the ratio of stone disease [20].

The New International Diabetes Federation (IDF) requires, Central obesity defined as waist circumference ≥90 cm in men and ≥80 cm in

women for Asians, except for Japanese) plus two of the following four factors [21]:

1. Raised Triglycerides ≥150 mg/dl (1.7mmol/L) or specific treatment for this lipid abnormality
2. Reduced HDL cholesterol <40 mg/dl (1.03mmol/l) in males and <50 mg/dl (1.29 mmol/L) in women or specific treatment for this lipid abnormality
3. Raised Fasting plasma glucose ≥100 mg/dl (5.6mmol/L) or previously diagnosed with type 2 diabetes
4. Raised Blood pressure (Systolic BP ≥130 or diastolic ≥ 85 mmHg or on treatment for previously diagnosed hypertension

Nephrolithiasis are polycrystalline aggregates containing various proportions of crystal and organic matrix components. The stone is mainly composed of chemical component calcium oxalate (50–70%), either in its pure form (30%) or mixed with calcium phosphate (40%). Uric acid (10–20%), struvite (ammonium-magnesium phosphate, 5–10%) and cystine (1–2%) stones are the other types of urinary stones. Stones are made of silica, xanthine and 2,8-dihydroxyadenine are rare. The composition of urinary calculi has changed in the last few years, because of increased rate of calcium-oxalate (from 65 to 80%) in the urine, while the rate of infection-related stone formation has decreased sharply from 15% to 4% [22]. This could be due to changes in lifestyle in developed countries and the widespread use of antibiotics. The epidemiology of cystine stones has not changed, due to persistence of homozygous cystinuria in a small proportion of the population [23]. The prevalence of uric acid stones has also dropped from 15 to 8%, this could be due to the early identification of metabolic alterations of patients and controlled dietary regimens in overweight patients [2].

Identifying a metabolic diagnosis or underlying cause for urolithiasis is very important. Significant underlying conditions which may predispose to an increased risk of formation of recurrent stones or cause other serious medical problems may be determined by the evaluation of a renal stone former [24]. Due to advances in the investigation modalities for the diagnosis of nephrolithiasis, stone disease was increasingly

diagnosed prior to their symptomatic presentation. The most important diagnostic tool that offers confirmation of the diagnosis is imaging, made based on the familial history, laboratory tests and physical examination. X ray, ultrasound, intravenous pyelography, CT scan, MRI and digital tomosynthesis can be used for the confirming diagnosis [25].

The medical treatment of urolithiasis may be divided into dietary and pharmacological interventions. The fluid intake can increase around 2.5 L per day to maintain a urine volume of >2 L is the cornerstone of management of urolithiasis in the majority of patient [26]. Maintaining dilute urine will prevent nucleation of supersaturated calcium oxalate and other poorly soluble salts (such as calcium phosphate and cystine) in the urine. Modification in dietary habits by taking fresh fruits and vegetables together with low-fat dairy products may be helpful. A low sodium version of this diet with a calorie and oxalate restriction seems sensible [27]. Non-steroidal anti-inflammatory drugs (NSAIDs) and opioids are the preferred classes of drugs for relieving pain associated with urolithiasis. Medical expulsive therapy (MET) is used to allow spontaneous expulsion of moderately sized distal ureteral calculi from the urinary tract. Alpha-adrenergic blockers or calcium channel blockers with or without corticosteroids are used for MET. Chemolytic dissolution therapy is a dissolution technique that aims at the dissolution and removal of urinary stones via pH alteration, chelation, and disulphide rearrangement [25]. And, due to marked advancement in technology, nephrolithiasis was increasingly treated by non-invasive methods like Extra corporal Lithotripsy (ESWL) and by minimal invasive procedures like Per Cutaneous Nephrolithotomy (PCNL). These procedures treat the nephrolithiasis patients with less morbidity and with good results [3].

Because of profound morbidity due to the disease and during treatment, loss of renal function with end stage renal disease in some neglected cases and increased cost of expenditure for diagnosis and treatment, there has been shift of focus from treatment to prevention of nephrolithiasis. Metabolic syndrome is a complex of medical disorders; when they occur together have clinical significance like increased risk

of developing cardiovascular disease, cerebrovascular accidents, diabetes mellitus (type two) and atherosclerosis. There are different definitions for defining metabolic syndrome and they all include the main components – obesity or waist circumference, hypertension, hyperlipidaemia, and hyperglycaemia [28].

The associations of metabolic syndrome with nephrolithiasis have been reported by many studies in a defined population. It has been shown to be associated with metabolic syndrome patient's urinary constituents like decrease in urinary PH, increased urinary calcium and uric acid excretion, and decreased excretion of urinary citrate which is an important inhibitor of nephrolithiasis [29].

Therefore, we proposed this study to evaluate the association between urolithiasis and metabolic syndrome.

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AIMS & OBJECTIVES

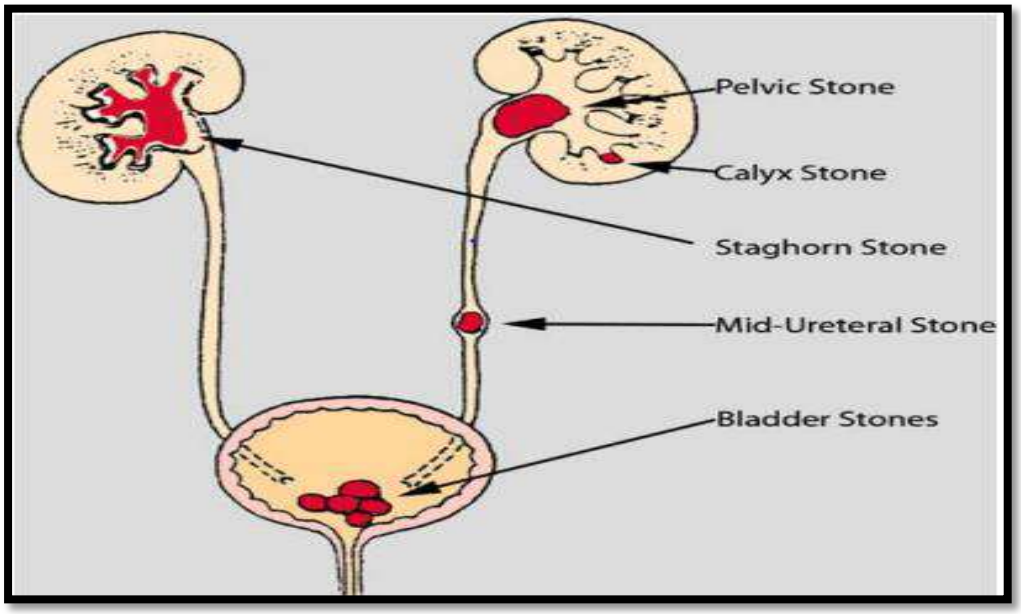
1. To evaluate the relationship of Urolithiasis with metabolic syndrome constituents.
2. To evaluate the biochemical component of stone in metabolic syndrome.

REVIEW OF LITERATURE

PATHOPHYSIOLOGY OF CALCULUS FORMATION:

The formation mechanism of urolithiasis is very complex; currently no single pathophysiological theory can properly describe urolithiasis formation with metabolic syndrome. Over the past decade, many studies have been done on the topic of pathophysiology of urolithiasis with metabolic syndrome and several hypotheses have been proposed [20].

Stones along the urinary tract can be in the kidneys, ureters, and urinary bladder. Kidney stones are divided as either staghorn or non-staghorn. Staghorn stones fill numerous major and minor calices while non-staghorn stones are characterized as calyceal or pelvic in location. Ureteral stones are defined as proximal, middle, or distal. Kidney stones having less than 5 mm in diameter have a high chance of being passed, while those of 5–7 mm in size have a 50% chance, and the kidney stones having size over 7 mm almost always require urological intervention. Renal colic (flank pain) starts as the stone begins its passage down the urinary tract. While approximately 90% of stones are successfully passed out of the urinary tract, the remaining stones generally must be surgically removed [30].



Picture 1: Location of staghorn and non-staghorn kidney stones [30]

Most kidney stones are calcium stones, with calcium oxalate (CaOx) and calcium phosphate (CaP) accounting for approximately 80% of all these stones, uric acid (UA) about 9%, and struvite (magnesium ammonium phosphate hexahydrate, from infection by bacteria that possess the enzyme urease) approximately 10%, leaving only 1% for all the rest (cystine, drug stones, ammonium acid urate)[30].The one point on which almost all urolithiasists agree that stones will not form if crystal of calcium oxalate do not nucleate within the kidney. Furthermore, nucleation will occur when the urine is supersaturated with calcium oxalate. The two most obvious determinants of urinary saturation with calcium oxalate are the renal outputs of calcium and oxalate. The amount of these substances are important but rather their concentration that will affect the likelihood of crystal nucleation, the throughput of water, or urinary volume, will also influence supersaturation [31].

The main cause of occurrence of stone can be attributed to an excessive urinary excretion of calcium (hypercalciuria), oxalate (hyperoxaluria) or urate (hyperuricosuria) or to an abnormally low output of citrate (hypocitraturia) or magnesium (hypomagnesuria). Dehydration, leading to a low volume of highly concentrated urine, can undoubtedly be resulted as the cause of stones on occasion, as can an elevated urinary pH such as occurs in renal tubular acidosis or infection [31]. Nephrolithiasis contains large amount of crystalline material (97%-98%) and organic matrix providing the framework for deposition of crystals [31].

Calculus formed when

1) There is excess excretion of calculus forming salts and precipitation to form nuclei or crystal.

2) There is decrease in substance that inhibits crystal deposition.

3) There is availability of specific macromolecules needed for calculus formation.

The calculus formation inhibitors present in urine were citrate, glycosaminoglycan like heparin sulphate, magnesium, RNA, acid

mucopolysaccharides and urinary glycoproteins like Tamm Horsfall glycoprotein and nephrocalcin.

Citrate was an important inhibitor of nephrolithiasis and it acts by

1) It reduces the calcium salts saturation in urine by combining with calcium.

2) Directly prevents calcium oxalate nucleation.

3) It inhibits precipitation and growth of Calcium Oxalate crystals.

4) It enhances Tamm Horsfall glycoprotein's inhibitory effect

These inhibitors allow high concentration of Calcium Oxalate crystals in the state of solution. This point of saturation was called as metastable state. It can be proposed that nephrolithiasis was formed from calcium salts in a metastable urine by heterogeneous nucleation.

Calculus analysis shows it contains crystalline and non-crystalline component. This non-crystalline component was termed as matrix. In nephrolithiasis the matrix commonly accounts to 2-3% [32].

The first evidence of crystal retention has been showed by Randall in1940 as plaques of sub epithelial deposits of calcium crystals in renal papillae. These plaques were called Randall's plaques which act as a nidus for urinary calculus formation. Nephrolithiasis contains mostly calcium (75%). So, it was classified in to calcium containing calculus and non-calcium containing calculus [33].

CALCIUM-CONTAINING CALCULUS

- Calcium oxalate – 60%
- Hydroxyapatite- 20%
- Brushite- 2%
- Uric acid – 7%

NON-CALCIUM CONTAINING CALCULUS

- Struvite – 7%
- Cystine -1%.

The derangements causing nephrolithiasis with calcium were due to hypercalciuria, hyperoxaluria, hyperuricosuria, and hypocitraturia. Cystine calculus was formed due defective absorption of renal cystine. Uric acid calculus was formed in acidic urine and Struvite calculus

formed in infective urine where urea splitting organisms like Proteus and Klebsiella cause urine alkalization and calculus formation.

CALCIUM CONTAINING CALCULUS

Hypercalciuria

Hypercalciuria has been one of the most frequently detected abnormalities found in persons having calcium containing nephrolithiasis. Increased calcium concentrations in urine causes increased urinary calcium salts saturation and reduced urinary calculus inhibitors like urinary citrate.

Pak et al [34] classified the causes of hypercalciuria into three types

- Absorptive hypercalciuria
- Renal hypercalciuria
- Resorptive hypercalciuria

Absorptive Hypercalciuria - defined as increased urinary calcium following oral calcium load due to increased intestinal absorption of calcium. It usually occurs in 55% of calculus forming patients. It can be classified into type 1- when urinary calcium excretion was high in spite of low calcium diet and type 2- when urinary calcium level becomes normal when patient was placed in calcium restricted diet.

Renal hypercalciuria - Of the reabsorbed 98% of filtered calcium, 70% of the absorption occurs in proximal tubule mostly by paracellular pathway. So impaired renal absorption leads to increased urinary calcium leads to secondary hyperparathyroidism. The exact cause of renal calcium leak was not found but may be due to renal injuries, structural abnormality, or functional defect.

Resorptive Hypercalciuria - is uncommon and mostly due to primary hyperparathyroidism.

Hyperoxaluria: when urinary oxalate excretion exceeds 40mg/day. Hyperoxaluria divided into 3 types [35]:

1) Primary hyperoxaluria - is caused by genetic defect in the glyoxalate metabolism, where normal metabolism of glyoxalate to glycine does not happen and there is increased oxidative conversion of

glyoxalate to oxalate occurs. It leads to increased (>100mgs/day) excretion of urinary oxalates.

2) Enteric hyperoxaluria - is caused by intestinal malabsorptive state as in inflammatory bowel disease, celiac sprue, intestinal resection surgeries or in bariatric surgeries done for obesity. It was the most common acquired form of hyperoxaluria.

3) Dietary hyperoxaluria- Diets rich in oxalates like nuts, spinach, strawberry, chocolate, broccoli, and rhubarb can cause hyperoxaluria [36].

Hyperuricosuria

Is defined as when uric acid excretion in urine exceeds 600mgs/day. The common causes of hyperuricosuria are increased purine intake in diet, gout, myeloproliferative disorder, lymphoproliferative disorder, multiple myeloma, pernicious anaemia, polycythaemia, thalassemia, partial or complete deficiency of enzyme hypoxanthine guanine phosphoribosyltransferase, enzyme phosphoribosylpyrophosphatesynthetase over activity and renal hypouricemia [37].

Hypocitraturia

Defined as when urinary citrate level is below 320mgs/day.

Uric acid stones

Uric acid stones are caused by three main determinants. They were low urine volume, low PH, and hyperuricosuria. Of these low urinary PH is very important and consistent variable for the formation of uric acid calculus.

Cystine calculus

Is caused by cystinuria which was an inherited autosomal recessive disease caused by disorder in intestinal and renal tubular transport of cystine, ornithine, lysine, and arginine.

Struvite calculus

Struvite or magnesium ammonium phosphate calculus was reported by Swedish geologist and named it as struvite after his mentor H.C.G.Von Struvite. It is formed as a result of urinary infection with urea splitting enzyme urease containing organism such as Proteus. Struvite or triple

calculus occurs more commonly in females in the ratio of 2:1 when compared to males.

The metabolic syndrome (MetS) is a collection of many interrelated risk factors carrying an increased risk of atherosclerotic cardiovascular disease, type 2 diabetes mellitus and all-cause mortality [38, 39]. Despite different definitions of MetS have been given, there is agreement regarding its main components: hypertension, obesity and disorders of carbohydrate and lipid metabolism (i.e., elevated serum triglyceride and apolipoprotein B, increased small LDL particles and a reduced level of HDL-cholesterol). Individuals with these characteristics commonly harbour a pro-inflammatory state, resulting in a pro-thrombotic condition [15]. The American Heart Association (AHA), the World Health Organization (WHO), the European Group for the Study of Insulin Resistance (EGIR) and the National Cholesterol Education Program—Third Adult Treatment Panel (NCEP ATP III) have similarities in the main components of metabolic syndrome: central obesity, hypertension, dyslipidaemia, and insulin resistance [40]. The WHO criteria for the diagnosis of metabolic syndrome require the presence of diabetes mellitus, impaired glucose tolerance, impaired fasting glucose, or insulin resistance, along with any 2 (or more) of the core components, for a patient to be considered as suffering from metabolic syndrome [20].

Recent epidemiological data have found that patients with metabolic syndrome are at high risk for chronic kidney diseases. In this scenario, some of the components of MetS have been associated with the occurrence of nephrolithiasis (NL) or with biochemical abnormalities that in turn are related to NL [15].

Cappuccio FP, and colleagues (1990) [41] considering the effect of potential confounding variables, they examined the hypothesis that kidney stone disease is more prevalent among hypertensive men. As part of the 10-year follow-up to a national survey of the prevalence of cardiovascular risk factors, a cross-sectional study was done on a sample of the male working population. The survey included 688 male workers aged 21-68. The interventions consisted of anthropometric and

blood pressure measures, blood tests, and the administration of a comprehensive questionnaire designed to detect a history of urolithiasis. The primary end measures were the prevalence of a history of urolithiasis among normotensive, untreated, and treated hypertensive males, adjusted for potential confounding effects of age, body mass index, renal function, serum urate, and total calcium concentrations. The results revealed that 509 of the 688 participants had normal blood pressure. Among the remaining, 118 had untreated hypertension, while 61 were treated. The frequency of urolithiasis in the general population was 16.3% (112/688). The relative risk of hypertensive participants having a history of kidney stones was double that of the normotensive group (odds ratio 2.11; 95% confidence interval 1.17 to 3.81) and increased when only treated hypertensives were evaluated (odds ratio 3.16; 95% confidence interval 1.75 to 5-71). 13.4% (68/509) of normotensive participants had a history of urolithiasis, compared to 20.3% (24/118) of untreated hypertensives and 32.8% (20/61) of treated hypertensives ($p<0.0001$). The age-adjusted relative risk for treated hypertensive males was greater than that for normotensive men (MantelHaenszel pooled estimate of odds ratio 2.63; 95% confidence interval 2.23 to 3.10). The conclusion of the study is that urolithiasis and hypertension are linked in a clinically significant manner. The increased urine calcium excretion typically observed in hypertension may be the connection in the pathogenesis.

Ekeruo WO, and co-workers (2004) [42] assessed the risk factors for stone development and the effect of selective medical therapy on recurrent stone formation in the obese patient group. The authors conducted a retrospective chart analysis to identify obese Stone Centre patients with stone disease. Both metabolic risk variables for stone formation and patient responsiveness to medical treatment were identified. A similar analysis was conducted on a sample of non-obese stone-formers of comparable age and gender. Results indicated that 14 % (140) of 1,021 patients were categorised as obese (body mass index greater than 30). 83 of these patients had comprehensive metabolic examinations, with a mean follow-up of 2.3 years. The most

prevalent metabolic abnormalities among these obese individuals were gouty diathesis (54%), hypocitraturia (54%), and hyperuricosuria (43%), all of which exhibited at considerably greater levels than those of the nonobese stone formers ($p< 0.05$). In 32 obese patients with accessible stone analysis, 63% had uric acid calculi. After commencing treatment with selective medical therapy, both obese and nonobese patients displayed normalisation of metabolic anomalies, resulting in a drop in the average number of new stones generated per patient per year from 1.75 to 0.15. Obesity, as a result of nutritional irresponsibility, probable purine gluttony, and possibly type II diabetes, appears to have a substantial influence in the production of recurrent stones, according to the results of the present study. In these patients, who are sometimes difficult to treat, a metabolic evaluation, medical treatment, and dietary recommendations to reduce animal protein consumption can greatly reduce the risk of recurrent stone formation.

Abate N, Chandalia M, and colleagues (2004) [43]determined whether insulin resistance relates to excessively low urine pH in obviously healthy volunteers (non-stone formers) and whether insulin resistance can explain excessively low urinary pH in patients with uric acid nephrolithiasis. A hyperinsulinemia euglycemic clamp, 24-hour urine investigations, and anthropometric measurements of adiposity were performed on 55 healthy volunteers (non-stone-formers) with a broad range of body mass index and 13 patients with recurrent uric acid nephrolithiasis. A subgroup of 35 non-stone formers underwent 2-hour timed urine collection prior to and during the hyper insulinemic phase of the clamp studies. Low insulin sensitivity, as indicated by glucose disposal rate, was strongly linked with low 24-hour urine pH in the non-stone former population ($r = 0.35$; $P = 0.01$). In addition to an acidic urine pH and hypouricosuria, individuals with recurrent uric acid nephrolithiasis exhibited substantial insulin resistance (glucose disposal rate: uric acid stone-formers versus normal; 4.1 ± 1.3 vs. 6.9 ± 2.1 mg/min/kg of lean body mass, $P = 0.008$). Acute hyperinsulinemia was related with an increase in urine pH (from 6.1 ± 0.7 at baseline to 6.8 ± 0.7 during hyperinsulinemia; $P< 0.0001$), urinary ammonia

excretion (from 2.7 ± 1.6 mEq/2 hr at baseline to 4.0 ± 2.6 mEq/2 hr during hyperinsulinemia; P = 0.002), and urinary citrate excretion (from 48 ± 33 mg/2 hr at baseline and 113 ± 68 mg/2hr p <0.0001). The study found that decreased urine ammonium and pH may be a renal indication of insulin resistance. Despite norm uricosuria, this deficiency can result in an elevated risk of uric acid precipitation.

Chen J, and colleagues (2004) [44] investigated the relationship between the metabolic syndrome and the risk of chronic renal disease and microalbuminuria. It was a cross-sectional investigation. In the chronic renal disease (n = 6217) and microalbuminuria (n = 6125) studies, participants older than 20 years of age were evaluated. The metabolic syndrome was characterised by the presence of three or more of the following risk factors: high blood pressure, low high-density lipoprotein cholesterol, high triglyceride level, raised glucose level, and abdominal obesity. Chronic renal disease was defined as a glomerular filtration rate of less than 60 mL/min per 1.73 m2 and microalbuminuria as a urine albumin–creatinine ratio between 30 and 300 mg/g. Multivariate-adjusted risk ratios of chronic kidney disease and microalbuminuria were 2.60 (95% confidence interval [CI], 1.68 to 4.03) and 1.89 (CI, 1.34 to 2.50), respectively, for people with the metabolic syndrome versus persons without the metabolic syndrome. Compared to participants with 0 or 1 component of the metabolic syndrome, participants with 2, 3, 4, and 5 components of chronic kidney disease had multivariate-adjusted odds ratios of 2.21 (95% confidence interval [CI], 1.16 to 4.24), 3.38 (95% confidence interval [CI], 1.48 to 7.69), 4.23 (95% confidence interval [CI], 2.06 to 8.03), and 5.85 (95% confidence interval [CI], 3.85 to 11.0), respectively. The multivariate-adjusted odds ratios of microalbuminuria for patients with 3, 4, and 5 components were 1.62 (95% confidence interval [CI], 1.10 to 2.38), 2.45 (95% confidence interval [CI], 1.55 to 3.85), and 3.19 (95% confidence interval [CI], 1.96 to 5.08), respectively. In conclusion, these results show that the metabolic syndrome may be a significant contributor to chronic renal disease.

Rendina D, and colleagues from Italy (2009) [15] examined the association between MetS and NL, as well as the relationship between MetS constituent parts and NL, taking into account the strong correlation between these two variables. They examined 2,132 Caucasian inpatients at the Spinelli Hospital in southern Italy (males/females = 0.95; mean age 63.8 ± 15.8 years; body mass index 26.1 ± 3.9 kg/m2). The MetS was diagnosed using the Heart Association/National Heart, Lung, and Blood Institute's criteria. The existence of NL was determined with an ultrasound scan of the kidneys and upper urinary tract. Seven hundred twenty-five patients, or 34.0%, were diagnosed with MetS, according to the findings. Two hundred twenty patients (10.3%) demonstrated echographic evidence of NL, while 199 subjects (9%) reported a history of NL. Echographic evidence of NL was independently associated with MetS, male gender, and a previous episode of NL (only in male participants). Among the specific components of MetS, high blood pressure and abdominal obesity (only in females) were individually associated with echographic evidence of NL. This study reported that MetS is substantially related with echographic indications of NL. A gender-related variation was also seen in the clinical manifestation of NL.

Kuk JL, Ardern CI (2010) [45] determined the prevalence of the various combinations of risk variables that comprise the metabolic syndrome, as defined by the National Cholesterol Education Program, and analysed their connection with all-cause mortality in younger and older men and women. Study participants were 2,784 men and 3,240 women from the Third National Health and Nutrition Examination Survey with public-access mortality data linkage (follow-up = 14.2 ± 0.2 years). Metabolic syndrome was present in 26% of younger participants (aged <65 years) and 55.0% of older participants (aged >65 years). The most prevalent metabolic syndrome combination was the clustering of high triglycerides, low HDL cholesterol, and high blood pressure in younger males (4.8%) and triglycerides, HDL cholesterol, and an increased waist circumference in younger women (4.2%). The most prevalent metabolic syndrome combination in older men (8.0%) and women

(9.2%) was the presence of all five metabolic syndrome components. The association between metabolic syndrome combinations and death varied. In younger adults, having all five characteristics of metabolic syndrome was most strongly related with mortality risk, whereas none of the metabolic syndrome combinations were associated with death in older males. In older women, excessive glucose, or low HDL as a component of metabolic syndrome was most strongly related with an increased risk of death. In conclusion, metabolic syndrome is a complex entity with age and sex differences in component clusters, which may have significant consequences for understanding the connection between metabolic syndrome and mortality risk. In assessing health and mortality risk, the metabolic syndrome may obfuscate significant distinctions.

Jeong IG, and colleagues in a cross-sectional study (2011) [46] analysed the relationship between metabolic syndrome and kidney stone production in a large screening group. The data was collected from 34,895 individuals who underwent general health screening tests at the Asan Medical centre between January 2006 and December 2006. National Cholesterol Education Program Adult Treatment Panel III, American Heart Association, and National Heart, Lung, and Blood Institute set the criteria for defining metabolic syndrome. Radiographic evidence of kidney stones was found in 839 (2.4%) of those tested, while metabolic syndrome was confirmed in 4,779 (13.7%). The multivariable-adjusted OR for kidney stones increased with waist circumference quintile and systolic/diastolic blood pressure quintet (P= 0.001). Age, gender, hypertension, and the presence or absence of metabolic syndrome were independent risk factors for kidney stones. The odds ratio (OR) for kidney stone prevalence was 1.25 (95% CI: 1.03-1.50) when metabolic syndrome was present. Adjusted for all factors, the odds ratio (OR) for the presence of kidney stones was 1.47 (95% CI: 1.25-1.71) among participants with hypertension versus those without hypertension. In conclusion, metabolic syndrome is significantly related with an elevated risk of kidney stone formation. Our findings indicate the need for interventional research to examine the impact of

preventing and treating metabolic syndrome on the risk of kidney stone formation.

Zhang Q, and colleagues (2012) [47] examined the UA-MetS correlations using data from a longitudinal study of male residents who underwent routine physical examinations at the Health Management centre of Shandong Provincial Hospital (HMCSPH). To further estimate this time-dependent association, they fitted a generalised estimating equation (GEE) regression model with data from a large-scale 6-year longitudinal study involving 2222 participants aged > 25 years with an average of 3.5 repeated measures of UA per individual at the Health Management centre of Shandong Provincial Hospital, Shandong, China. After controlling for other potential confounding factors (total cholesterol, low-density lipoprotein), it was determined that time-dependent UA level was an independent risk factor for MetS (OR = 1.6920, p< 0.0001). The UA level was found to be positively related to obesity, hypertension, and dyslipidaemia, but negatively related to hyperglycaemia. The study concluded that serum UA concentration may be a significant MetS risk factor. Moreover, their research indicated that UA level is an independent risk factor for obesity, hypertension, and dyslipidaemia, but a protective factor for hyperglycaemia. These findings are consistent with those of other studies on Asian populations and provide a foundation for developing a MetS risk assessment model in China utilising UA levels and other parameters.

Kim YJ, and colleagues from Korea (2013) [48] this study assessed the relationship between metabolic syndrome and nephrolithiasis. Data were collected from 116,536 persons who performed health screening examinations at a health promotion facility in Seoul, Korea, between January 2010 and December 2010. All respondents were requested to complete a questionnaire regarding their medical history. On each participant, anthropometric and biochemical measurements were taken. Abdominal ultrasonography was used to assess the presence of NL. The subjects were divided into MetS and non-MetS groups based on the MetS criteria (National Cholesterol Education Program Adult

Treatment Panel III). Using multivariable logistic regression analysis, they computed the Odds Ratios (ORs) and 95% Confidence Intervals (CIs) for the existence of NL in the MetS group relative to the non-MetS group, controlling for age, blood levels of creatinine and uric acid, and past medical history of NL. In the NL group, the prevalence of MetS was 15.9% (N = 1129/7107) and in the non-NL group, it was 11.2% (N = 12,287/109,429), respectively. After correcting for potential confounding factors, male MetS patients were more likely to have NL than non-MetS participants (OR 1.11; 95% CI 1.02–1.20; p=0.01). Only elevated blood pressure (BP) was significantly associated with the existence of NL among MetS components (male; OR 1.08; 95% CI 1.01–1.15; p=0.043; female; OR 1.24; 95% CI 1.08–1.42; p=0.002). The presence of NL was considerably higher in male individuals as the number of MetS components rose (P for trend< 0.001), but not in female subjects (P for trend = 0.961). The conclusion of the present investigation was that NL was related with MetS and high BP.

Kohjimoto Y, and colleagues from Japan (2013) [49] analysed the relationship between the number of metabolic syndrome features and the severity of kidney stone illness, as measured by the number of existing stones and the number of stone episodes, as well as anomalies in urine components, using a nationally representative sample of Japanese patients with kidney stones. In 2005, the 6th Nationwide Survey on Urolithiasis in Japan collected data from 30,448 patients who participated in cross-sectional analysis. Patients with lower urinary tract stones, struvite stones, cysteine stones, or hyperparathyroidism were excluded, as were those younger than 15 years. Number of metabolic syndrome characteristics (obesity [BMI of 25 kg/m2], diabetes, hypertension, and dyslipidaemia) was a predictor. There were 11,555 patients included in the final analysis. The percentages of patients with recurring and/or numerous stones were 57.7%, 61.7%, 65.2%, 69.3%, and 73.3%, respectively, with 0, 1, 2, 3, and 4 metabolic syndrome features (P< 0.001). After adjusting for age and gender, there was a significant and stepwise rise in the likelihood of recurrent and/or numerous stones. In patients with four metabolic

syndrome characteristics, the chances were 1.8 times greater than in individuals with none (OR, 1.78; 95% CI, 1.22 to 2.42). In addition, after adjusting for age and gender, the presence of metabolic syndrome features was related with significantly higher probabilities of hypercalciuria, hyperuricosuria, hyperoxaluria, and hypocitraturia. Clustering of metabolic syndrome traits is associated with more severe kidney stone disease, increased urine calcium, uric acid, and oxalate excretion, and decreased urinary citrate excretion, according to the findings of a study. These findings show that kidney stone disease is a systemic illness associated with metabolic syndrome.

Besiroglu H, Otunctemur A, Ozbek E (2014) [13] investigated the relationship between metabolic syndrome (MetS) and urolithiasis. Observational studies and reviews indicate a correlation between the prevalence of urolithiasis and MetS. However, additional research is required to reach a result that is more dependable and accurate. The authors conducted a search of the PubMed–Medline and Embase databases through February 2014 to discover urolithiasis and metabolic syndrome-related articles. Three authors independently extracted data on the study's design, participant characteristics, exposure and outcome assessments, and method employed to account for any confounding variables. For the estimation of risk, a random-effects model was applied. The meta-analysis of five controlled cross-sectional studies revealed a substantial connection between urolithiasis and MetS, with an overall OR of 1.39 (1.14–1.70). Patients with metabolic syndrome have an increased chance of developing urolithiasis, suggesting that this condition should be evaluated as a systemic issue. However, prospective, randomised investigations are necessary to evaluate these observations.

Liu YT, and colleagues (2017) [50] analysed the relationship between nephrolithiasis and metabolic syndrome, as well as its constituents in 2010 in 3793 subjects by a cross-sectional study was done in the Health Examination Department of a medical centre in Changhua, Taiwan. They investigated the medical records of individuals who had visited Changjia Christian Hospital's Health Examination centre in

2010. According to the exclusion criteria, individuals with an abnormal renal function and a minimum age of 20 were excluded. The findings revealed a link between nephrolithiasis, metabolic syndrome, and its components. The odds ratio (OR) (95% confidence interval [CI]) of metabolic syndrome for nephrolithiasis was 1.318 (1.083–1.604) with a significance level of 0.006. Greater waist circumference (multivariable-adjusted OR 1.338; 95% CI 1.098–1.631; P=0.004), elevated blood pressure (multivariable-adjusted OR 1.333; 95% CI 1.106–1.607; P=0.003), and elevated fasting glucose (multivariable-adjusted OR 1.276; 95% CI 1.054–1.546; P=0.01) were associated with nephrolithiasis. In conclusion, the mechanism is contested, and other possibilities are presented. The prevention of nephrolithiasis may be aided by both the alteration of one's lifestyle and the management of metabolic syndrome.

Yu WW, and co-workers (2019) [51] analysed the connections between MetS combinations and its individual components and all-cause mortality, as well as differences in the association by age and sex. The sample consisted of 82,717 adults from seven U.S. cohorts. MetS was present in 32% of males, 34% of women, 28% of younger persons (18–65 years), and 62% of older adults (>65 years) in the sample, with 14,989 fatalities during 14.6 ± 7.4 years of follow-up. In younger persons, the greater the number of MetS risk factors, the greater the risk of death from all causes. However, in older adults, only the presence of all five MetS risk factors was significantly linked with mortality. High blood pressure was the MetS factor most consistently present in MetS combinations that were significantly and strongly related with death, regardless of age or gender. In fact, in the absence of additional risk factors, high blood pressure was substantially linked with mortality in males (HR, 95% CI = 1.56, 1.33–1.84), women (HR = 1.62, 1.44–1.81), and younger adults (HR = 1.61, 1.45–1.79). In contrast, waist circumference, hyperglycaemia, and triglycerides were not independently related to death (p>0.05). The study concluded that across a broad U.S. population, the relationships between different MetS component combinations and all-cause mortality vary greatly.

Men, women, and younger persons with MetS combinations containing hypertension had larger connections with increased mortality risk, while older adults had negligible associations between MetS and mortality risk. Therefore, the authors propose that future algorithms may wish to incorporate differential weighting of these common metabolic risk markers, especially in younger populations.

Rams K, and colleagues from India (2020) [52] evaluated the Indian patients for the connection between metabolic syndrome and its components and urolithiasis. Patients with urolithiasis older than 18 years were enrolled in a prospective, cross-sectional observational study. Analysis was conducted on demographic information, body mass index (BMI), waist circumference, blood pressure, and laboratory data. 1200 urolithiasis patients were separated into two groups: those with [n = 208] and those without [n = 992] metabolic syndrome. The population's mean age was 47.26 (14.68), with 721 males and 479 females. The results revealed that the mean height, weight, and BMI of the two groups were considerably different (P< 0.001). In patients with metabolic syndrome, the proportion of obese patients (BMI >25), the proportion of patients with hyperuricemia, the waist circumference, blood pressure, triglyceride, and fasting blood sugar (FBS) levels were significantly higher; however, high density lipoprotein (HDL) levels were significantly lower (P< 0.001). With an increase in the number of metabolic components, a trend of considerably increasing waist circumference, triglycerides, FBS, systolic and diastolic blood pressure, and a tendency of significantly lowering HDL were detected (P< 0.001). Female patients were 19.6 times more likely than male patients to have metabolic syndrome (P< 0.001). Increasing waist circumference, triglycerides, FBS, and blood pressure were related to a higher risk of metabolic syndrome (P< 0.05). Reducing HDL was linked to a decreased risk of metabolic syndrome. Patients with hyperuricemia had a 5.68-fold increased risk of metabolic syndrome (P = 0.006). This study suggests that metabolic syndrome and its components are significantly associated with urolithiasis.

Rahman IA, and colleagues (2021) [53] aimed to clarify the relationships between MetS and its components and the occurrence of kidney stones. From January 1998 to October 2020, the online databases EMBASE, MEDLINE, and Google Scholar were searched for observational studies exploring the link between metabolic syndrome components and kidney stone incidence. To examine the connection, a Bayesian random effects meta-analysis and meta-regression were conducted. To determine the direction of the connection, a dose-response study was done. STATA and R statistics were used for data analysis. Eventually, a total of 25 possibly relevant studies (n = 934,588 people) were discovered. Metabolic syndrome was related with an elevated risk of nephrolithiasis with an odds ratio (OR) of 1.76 (95% confidence interval [CI]: 1.386-2.35). The summary odds ratios of hypertension and dyslipidaemia for having nephrolithiasis were 1.613 (95% confidence interval [CI]: 1.213 – 2.169) and 1.586 (95% CI: 1.007 – 2.502). The odds ratios for diabetes and obesity were 1.552 (95% CI: 1.027-2.344) and 1.531 (95% CI: 1.099-2.110), respectively. Increasing the number of MetS characteristics increases the likelihood of developing nephrolithiasis; the higher the fasting plasma glucose and body mass index, the greater the risk of kidney stone occurrence. Hypertension, diabetes, obesity, and dyslipidaemia relate to an increased risk of developing nephrolithiasis, according to the findings of the present study. Our investigation indicated a substantial linear connection between MetS components and nephrolithiasis, supporting the hypothesis that should be regarded a systemic illness.

Karoli R, and colleagues (2021) [54] examined the relationship between nephrolithiasis risk factors and metabolic syndrome. In a hospital-based case-control research, the presence of nephrolithiasis risk variables was evaluated in one hundred IDF-diagnosed metabolic syndrome patients and one hundred age- and gender-matched controls. Patients with metabolic syndrome were shown to have significantly elevated levels of uricosuria, hypercalciuria, oxaluria, and hypocitraturia. The prevalence of nephrolithiasis risk factors was

likewise elevated in patients with metabolic syndrome. 40% of patients exhibited low urine pH, with a mean pH of 5.8 ±1.6. 33% had hyperuricemia, 29% had hypercalciuria, and 15% had oxaluria, among other variables. Hypocitraturia was present in 13% and hyperuricosuria in 10%. There was a significant association between nephrolithiasis risk variables and metabolic syndrome components. In conclusion, the present investigation shows evidence of a link between nephrolithiasis risk factors and metabolic syndrome, suggesting that nephrolithiasis may be a systemic condition involving the interaction of numerous metabolic derangements. Determining prevalent modifiable risk factors for the formation of kidney stones could lead to the discovery of novel preventative measures.

MATERIALS AND METHODS

STUDY DESIGN - The study design was a Cross-sectional study.

SOURCE OF DATA:

The study was conducted among the patients admitted to department of Urology, Dayanand Medical College and Hospital, Ludhiana from August 2021 to January 2023.

INCLUSION CRITERIA

1. Age ≥ 18 years.
2. Either gender.
3. Patients with unilateral or bilateral Urolithiasis.

EXCLUSION CRITERIA

1. Patients with congenital renal abnormalities.
2. Chronic renal failure patients.
3. Patients with metabolic bone disorder or taking treatment for osteoporosis.
4. Patients with major debilitating disease like cancer.
5. Pregnancy.

METHOD OF COLLECTION OF DATA:

Information was collected through a pre- designed Performa for each patient chosen to be a part of the study with demographics, detailed history, clinical examination, and complete investigational workup. Details of the study was explained to each case and pre-informed consent from each patient was taken.

Patient who gave consent to participate in the study and not having any above-mentioned exclusion criteria were included in the study.

All individuals underwent ultrasound evaluation/ NCCT KUB of both kidneys.

All patients were assessed for measurement of waist circumference, their systolic and diastolic blood pressure, fasting blood sugar, serum triglycerides and serum HDL cholesterol levels.

Measurements was according to The New International Diabetes Federation (IDF) which requires,

Central obesity defined as waist circumference ≥90 cm in men and ≥80 cm in women for Asians, except for Japanese)

Plus, two of the following four factors:

1. Raised Triglycerides ≥150 mg/dl (1.7mmol/L) or specific treatment for this lipid abnormality.
2. Reduced HDL cholesterol <40 mg/dl (1.03 mmol/L) in males and <50 mg/dl (1.29 mmol/L) in women or specific treatment for this lipid abnormality.
3. Raised Fasting plasma glucose ≥100 mg/dl (5.6 mmol/L) or previously diagnosed with type 2 diabetes.
4. Raised Blood pressure (Systolic BP ≥130 or diastolic ≥ 85 mmHg or on treatment for previously diagnosed hypertension.

Ultrasonogram /NCCT KUB

All patients including all cases underwent ultrasonogram/NCCT KUB.

Waist circumference

Waist circumference was measured using a non-stretchable measuring plastic tape. The measurement was taken with the individuals in a relaxed and standing position with both feet together. Waist circumference measured at midpoint of lowermost border of twelfth rib and upper border of iliac crest at the end of expiration.

Measurement of Blood Pressure

Systolic and diastolic BP was measured using digital sphygmomanometer. Blood pressure was obtained with the individuals in calm and sitting position. Two readings were taken with five minutes apart and their average was taken into consideration.

Stone Analysis

After surgery stone sample of metabolic syndrome patient was sent for stone analysis for composition of stone after obtaining consent from patients.

SAMPLE SIZE – Sample size was 180 patients (Time bound).

DURATION OF STUDY –August 2021 to January 2023.

OUTCOME- The outcome of the study was defined as significant association of metabolic component as a risk factor for stone formation in patient with metabolic syndrome and common composition of stone in the patient with metabolic syndrome.

STATISTICAL ANALYSIS

Data was described in terms of range, mean ±, standard deviation, frequencies (number of cases) and relative frequencies (percentages)

For discrete data -proportion is computed and the mean and standard deviation was computed for the continuous data. The chi square test was applied to compare the proportions between the groups to assess the statistical significance. All analyses were two tailed and $p < 0.05$ was considered significant. SPSS version 21.0 was used for data analysis.

OBSERVATION & RESULTS

This study was undertaken in the Department of Urology at DMC&H Ludhiana, 180 subjects consented to participate in our study. The characteristics of subject's included in our study are mentioned below. All were evaluated for metabolic syndrome.

Table 1: Descriptive Statistics of study population

	N	Minimum	Maximum	Mean	Std. Deviation
Age	180	19.00	75.00	46.27	12.72
BMI	180	16.10	33.80	24.74	4.92
Waist Circumference(cm)	180	56.00	120.00	85.06	12.13
SBP (mmHg)	180	90.00	170.00	126.38	16.94
DBP (mmHg)	180	60.00	110.00	80.18	11.46
FBS (mg/dl)	180	50.00	210.00	105.49	37.02
TG (mg/dl)	180	86.00	266.00	140.86	31.48
HDL (mg/dl)	180	25.00	88.00	51.06	10.88

Mean age of patients was 46.27 ± 12.7 years. Mean BMI was 24.74 ± 4.92 kg/m2. Mean waist circumference of patient in our study was 85.06 ± 12.13 cm. Mean SBP and DBP were 126.38 ± 16.94 and 80.18 ±11.46 mmHg. Mean fasting blood sugar of our study population was 105.49 ± 37.02 mg/dl. Mean TG and HDL were 140.86 ± 31.48 and 51.06 ± 10.88 mg/dl respectively. Out of 180 patients 65, 59 and 25 patients were on antihypertensive, hypoglycaemic agents and lipid lowering drugs respectively.

Table 2: Sex distribution of study participants

Sex	Frequency	Percent
Female	51	28.3%
Male	129	71.7%
Total	180	100.0%

A total of 180 subjects studied 51 were female and 129 were male patients.

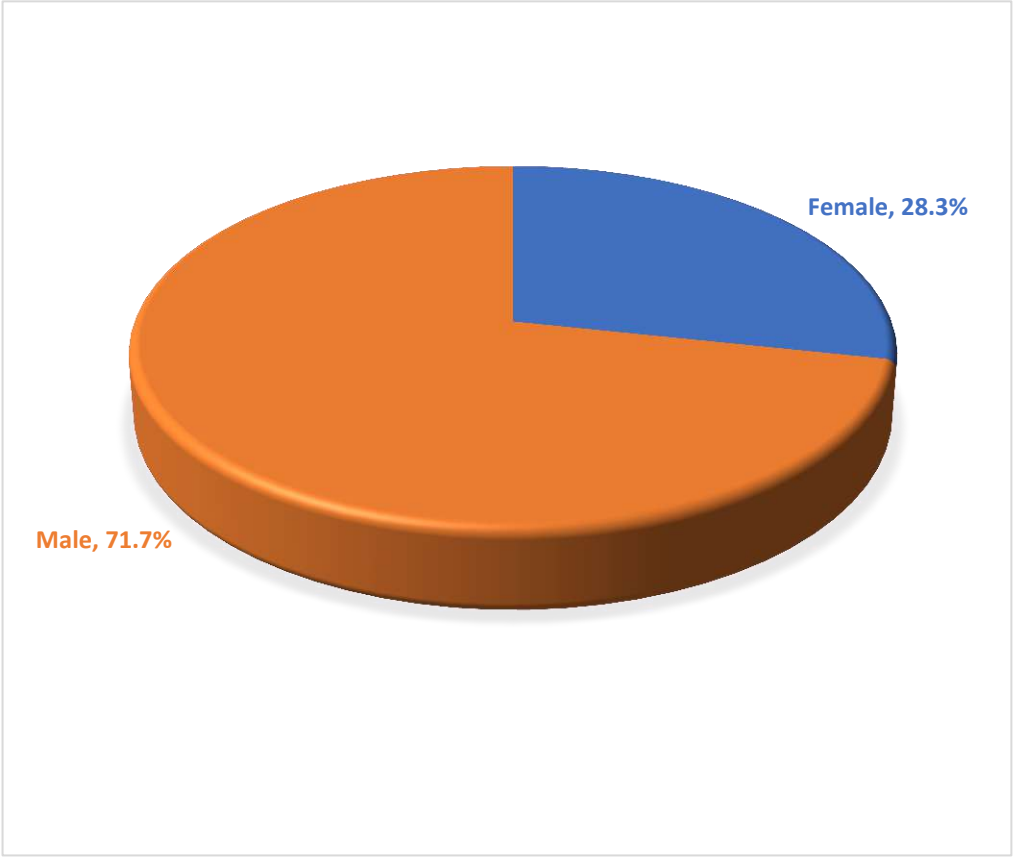


Figure 1: Pie chart showing male to female ratio of study population.

Table 3: Age distribution of study participants.

Age Group(years)	Frequency	Percent
<=30	20	11.0%
31-40	86	47.8%
41-50	46	25.6%
> 50	28	15.6%
Total	180	100.0%

Out of 180 patients in our study minimum age of participation was 19 years while maximum age was 75 years. Maximum patient was under age group of 31-40 years i.e., 86(47.8%) followed by between 41-50 years i.e., 46(25.6%).

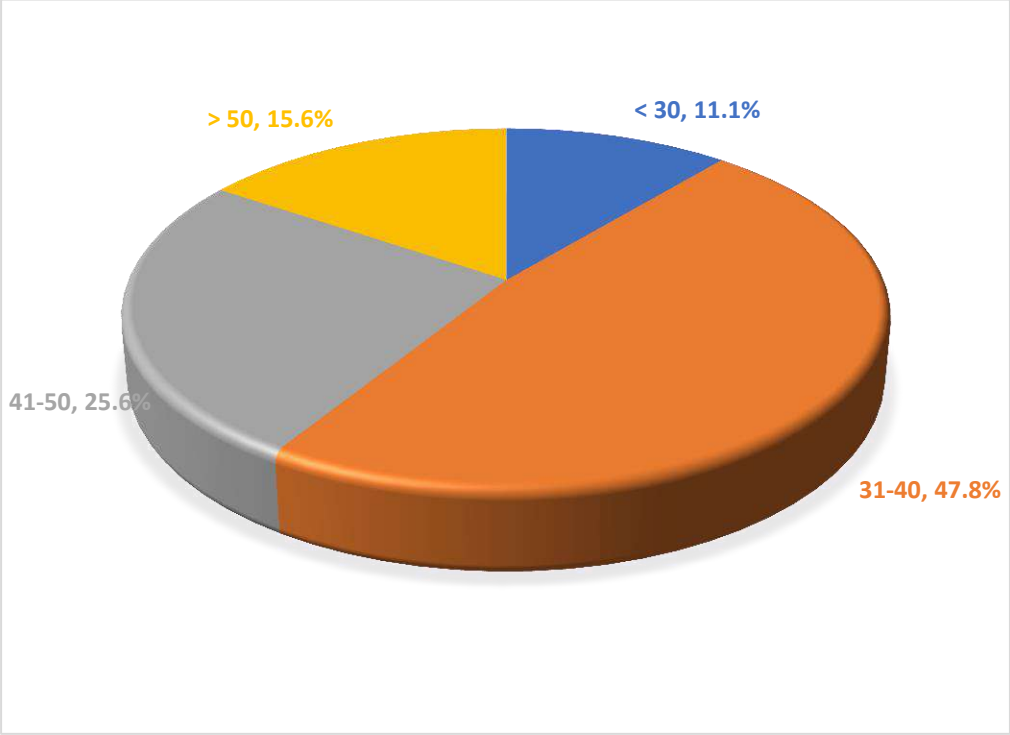


Figure 2: Pie chart showing age distribution of study population.

Table 4: Stone location distribution of study participants.

Stone Location	Frequency	Percent
Bilateral	24	13.3%
Left	61	33.9%
Right	88	48.9%
Vesical	7	3.9%
Total	180	100.0%

Out of 180 patients, left side stones were present in 61 patients (33.9%) Right side in 88 patients (48.9%) Bilateral in case of 24 patients (13.3%) and Vesical in only 7 patients (3.9%).

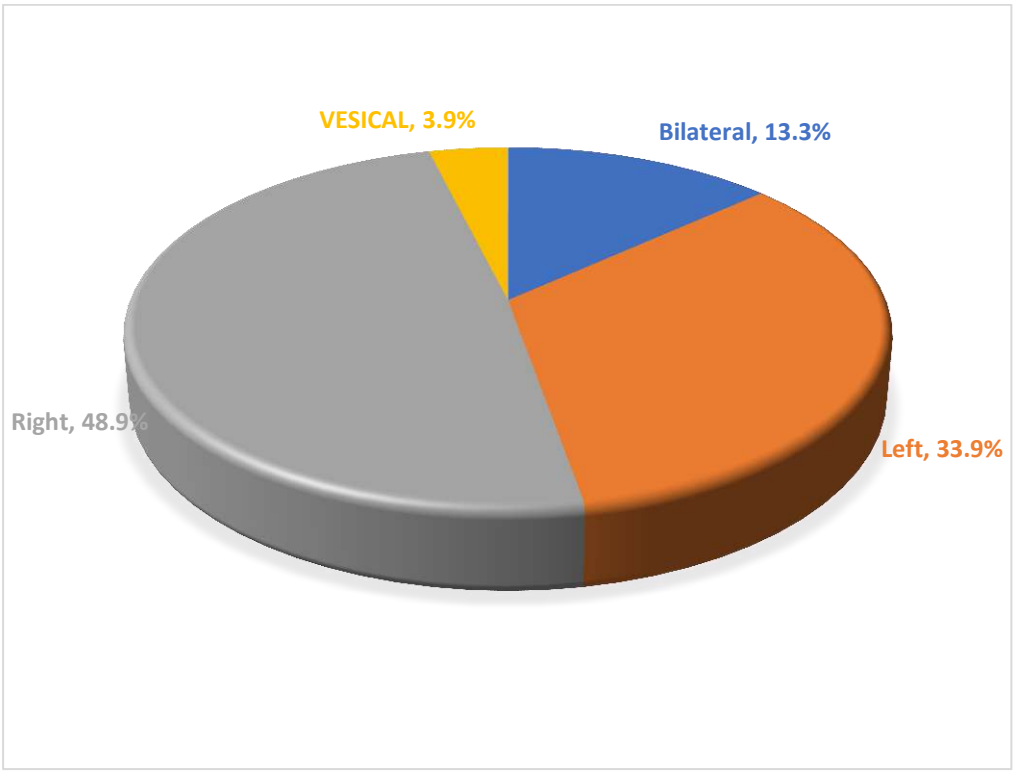


Figure 3: Pie chart showing stone location distribution of study population.

Table 5: BMI distribution of study participants.

BMI (kg/m2)	Frequency	Percent
< 18.5	9	5.0%
18.6-24.9	86	47.8%
25-29.9	40	22.2%
> 30	45	25.0%
Total	180	100.0%

Out of 180 patients, 9 patients (5%) were underweight, 86 patients (47.8%) were normal weight, 40 patients (22.2%) were overweight and 45 patients (25%) were in obese category

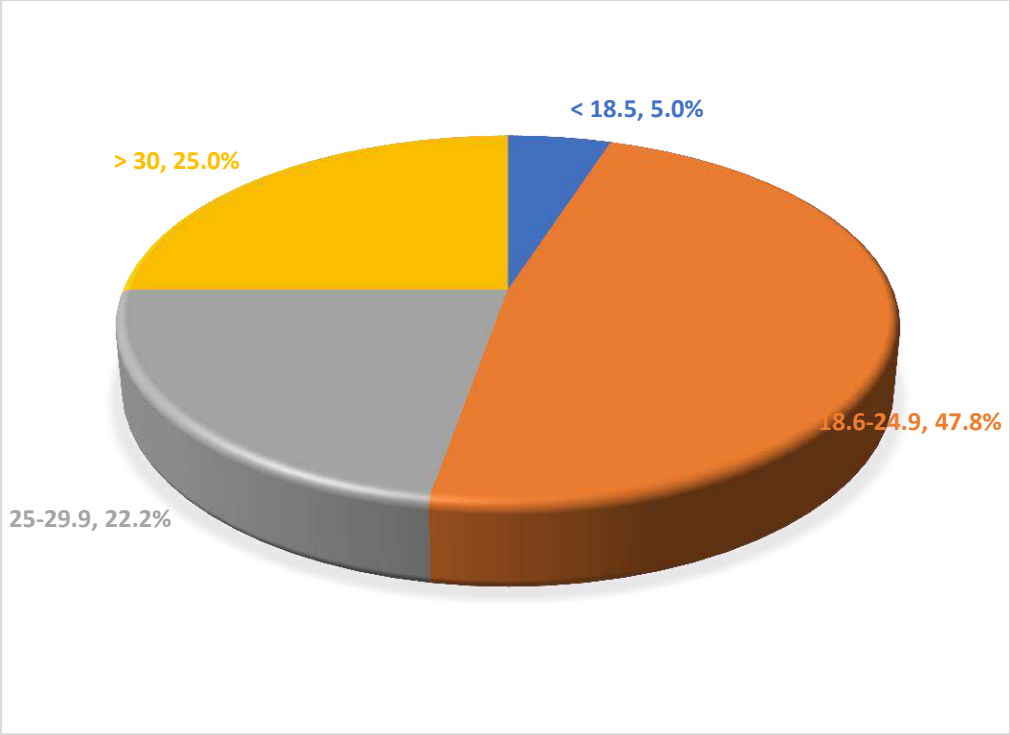


Figure 4: Pie chart showing BMI distribution of study population.

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Table 6: Waist circumference category of study participants.

Waist Circumference	Frequency	Percent
male>=90cm, female>=80cm	57	31.7%
male<90cm, female<80cm	123	68.3%
Total	180	100.0%

57 patients (31.7%) waist circumference were above cut off (male>=90cm, female>=80cm) for diagnosis of metabolic syndrome according to IDF criteria.

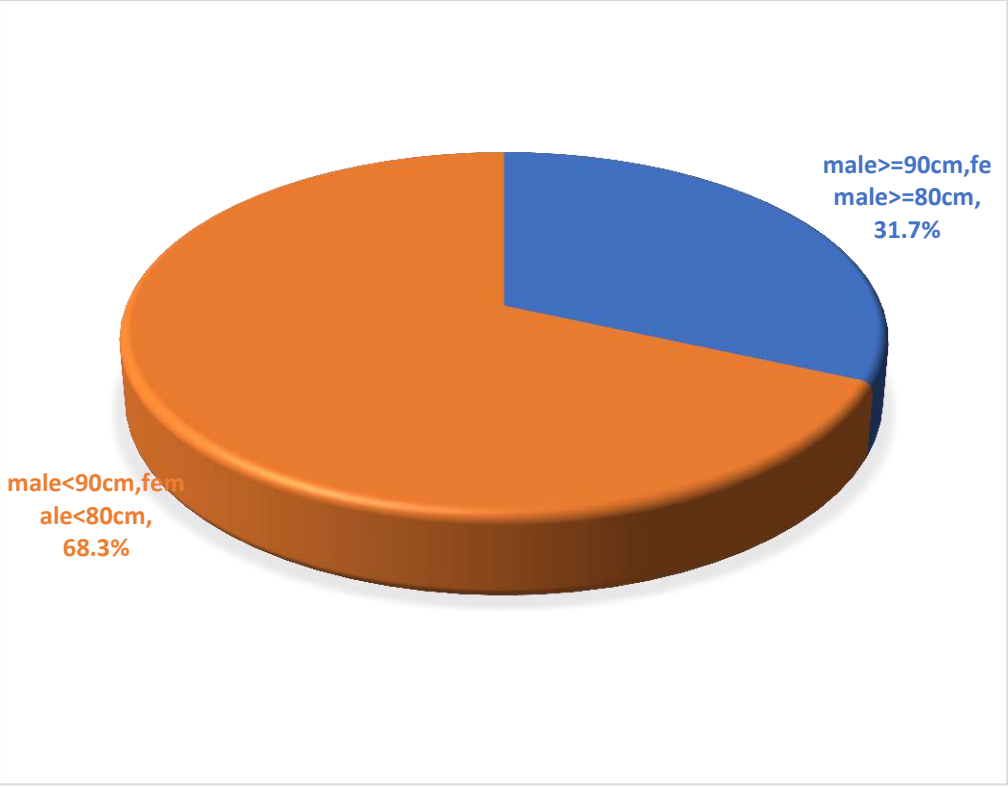

Figure 5: Pie chart showing waist circumference component distribution of study population.

Table 7: Blood pressure component category of study participants.

Blood Pressure	Frequency	Percent
SBP>=130 or DBP>=85mmHg or on treatment	81	45.0%
SBP<130 or DBP<85mmHg	99	55.0%
Total	180	100.0%

Out of 180 patient, 81 patients (45%) had Blood pressure component according to IDF criteria (SBP>=130 or DBP>=85mmHg or on treatment). Out of 81 patients 65 were already diagnosed to have hypertension and were taking Antihypertensive drugs.

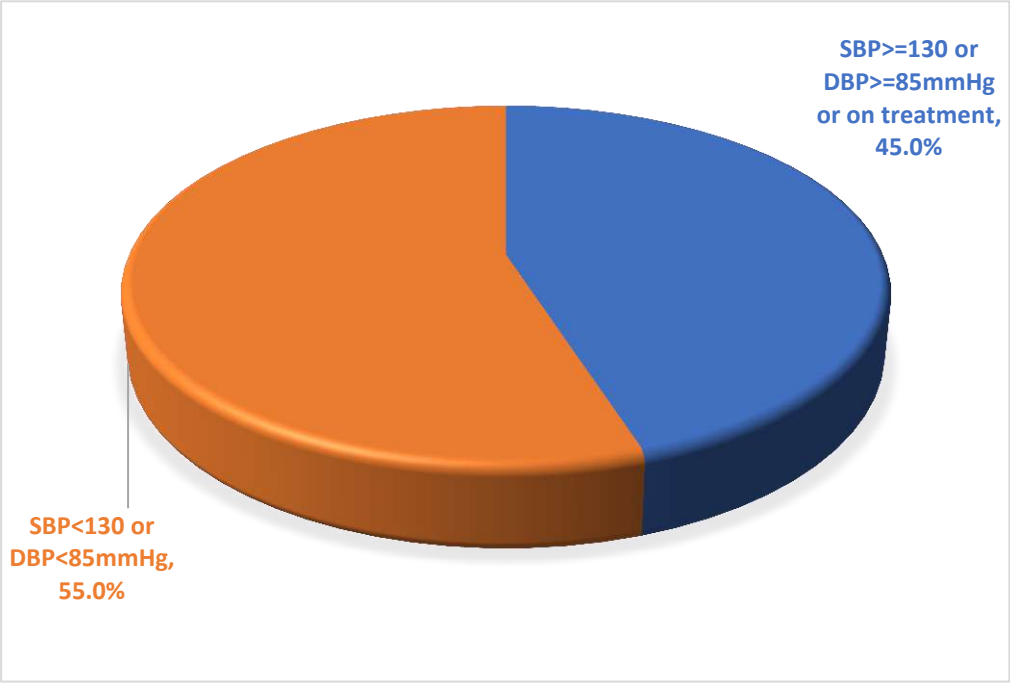

Figure 6: Pie chart showing Blood pressure component distribution of study population.

Table 8: Fasting blood sugar component category of study participants.

Fasting Blood Sugar	Frequency	Percent
>= 100mg/dl or on treatment	70	38.9%
< 100mg/dl	110	61.1%
Total	180	100.0%

70 patients (38.9%) out of 180 have Fasting blood sugar component according to IDF criteria (>= 100mg/dl or on treatment) and 59 of them were known case of Type 2 Diabetes Mellitus and were on treatment.

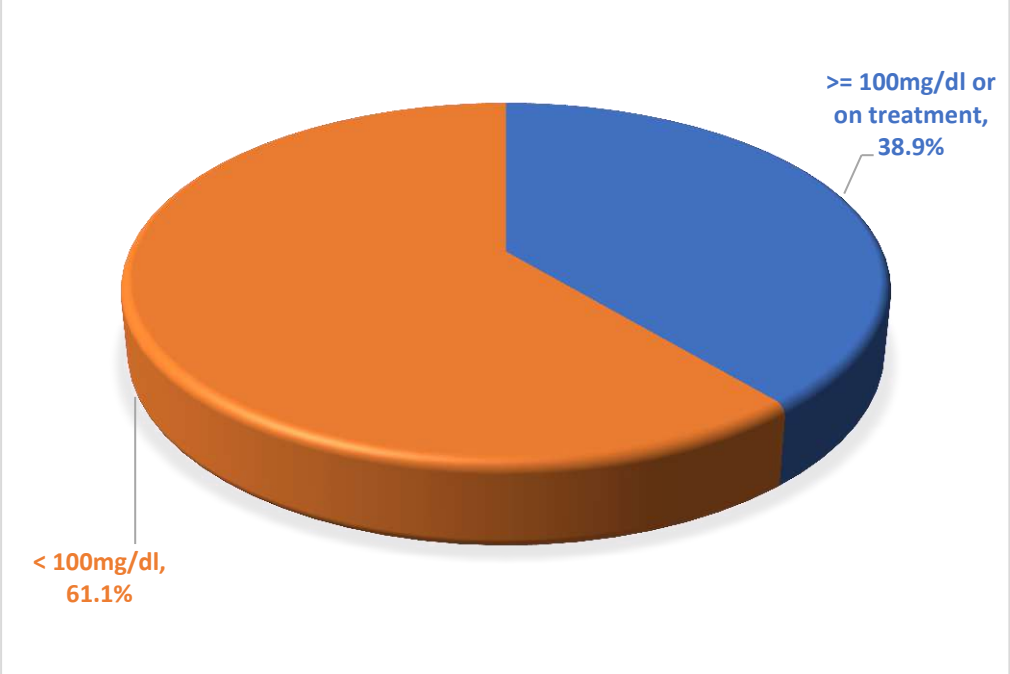

Figure 7: Pie chart showing Fasting blood sugar component distribution of study population.

Table 9: Triglycerides component category of study participants.

Triglycerides	Frequency	Percent
>= 150 mg/dl or on specific treatment for lipid abnormality	50	27.8%
< 150mg/dl	130	72.2%
Total	180	100.0%

50 patients (27.8%) had Triglycerides component as per IDF criteria for diagnosis of metabolic syndrome (>= 150 mg/dl or on specific treatment for lipid abnormality) and 25 out of 50 patients were on treatment for lipid abnormality.

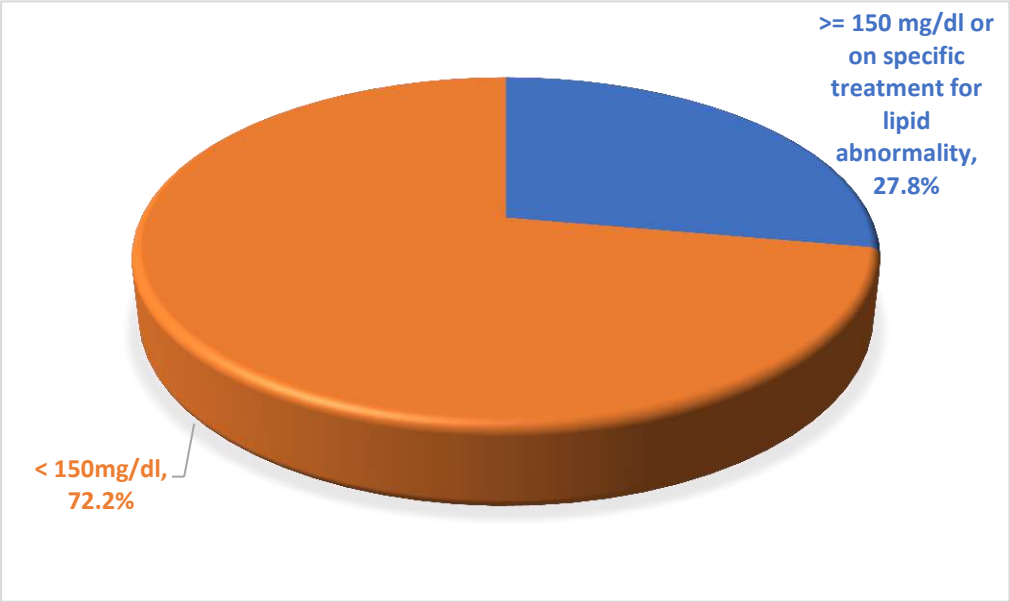

Figure 8: Pie chart showing Triglycerides component distribution of study population.

Table 10: HDL component category of study participants.

HDL	Frequency	Percent
males<40 mg/dl, female < 50mg/dl or on specific treatment for lipid abnormality	46	25.6%
males>=40 mg/dl, female >=50mg/dl	134	74.4%
Total	180	100.0%

46 patients (25.6%) had HDL component as per IDF criteria for diagnosis of metabolic syndrome (males<40 mg/dl, female < 50mg/dl or on specific treatment for lipid abnormality) and 25 out of 50 patients were on treatment for lipid abnormality.

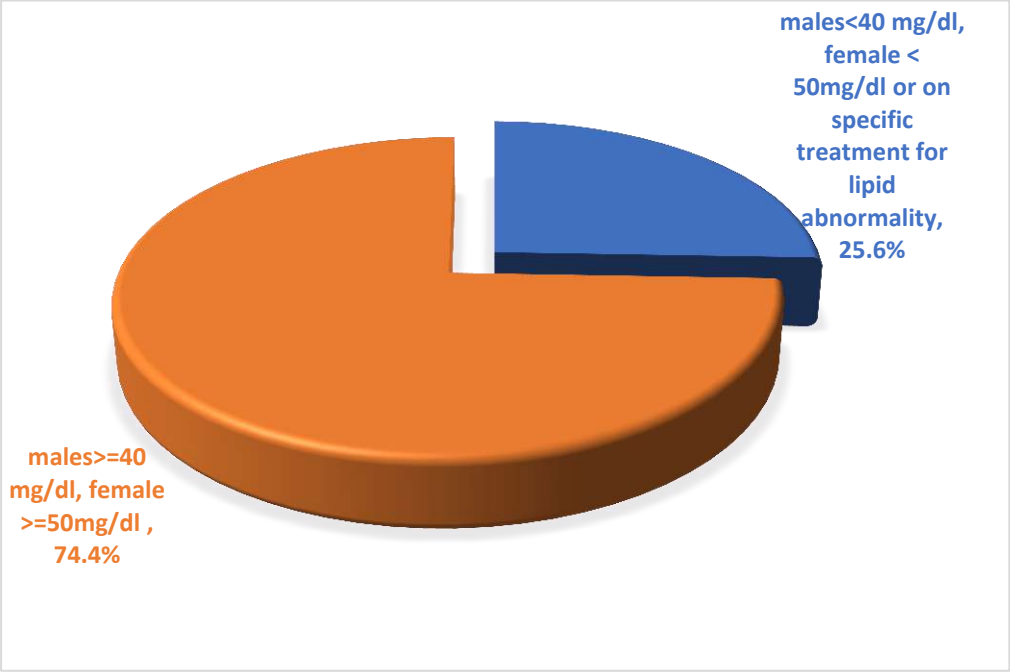

Figure 9: Pie chart showing HDL component distribution of study population.

Table11: Incidence of metabolic syndrome.

Patient group	Frequency	Percent
No metabolic syndrome	159	88.3%
Metabolic syndrome	21	11.7%
Total	180	100.0%

21 Patients (11.7%) were diagnosed to have Metabolic Syndrome as per IDF criteria.

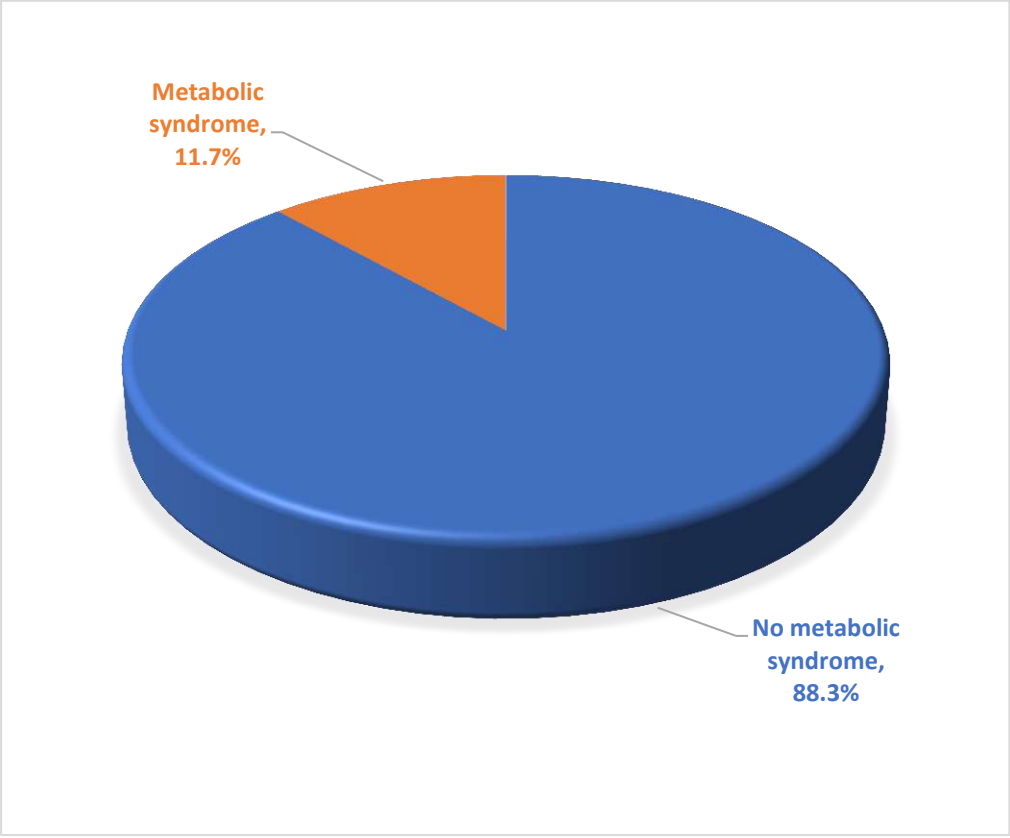

Figure 10: Pie chart showing incidence of metabolic syndrome patient in study population.

Table 12: Sex distribution of study participants between non-metabolic syndrome and metabolic syndrome group.

		Patient group				Total	Chi-square value	p-value
Sex		Non MetS		MetS				
	Female	42	26.4%	9	42.9%	51	2.47	0.116
	Male	117	73.6%	12	57.1%	129		
Total		159	100%	21	100%	180		

Out of 159 patients in non-MetS group 42(26.4%) and 117(73.6%) were female and male respectively, whereas in 21 patients of MetS group 9(42.9%) and 12(57.1%) were female and male respectively. The gender difference between two groups was comparable and was statistically insignificant (p value>0.05).

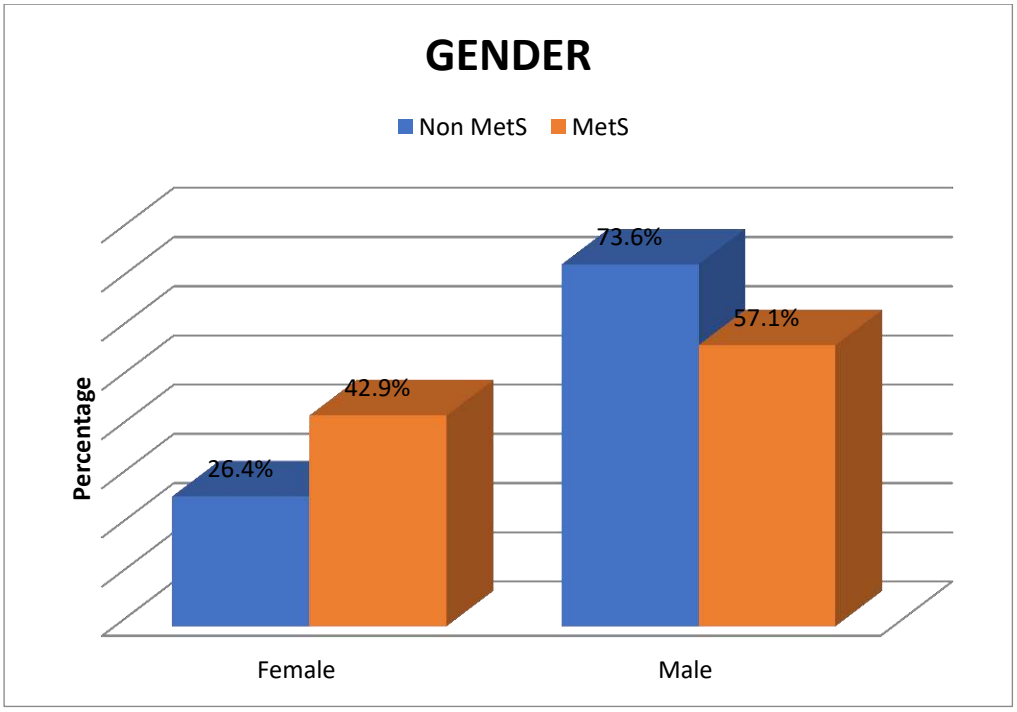

Figure 11: Bar diagram showing gender distribution of study participants between non-metabolic syndrome and metabolic syndrome group.

Table 13: Age distribution of study participants between non-metabolic syndrome and metabolic syndrome group.

		Patient group				Total	Chi-square value	p-value
		Non MetS		MetS				
Age Group (years)	< 30	19	11.9%	1	4.7%	20	4.003	0.261
	31-40	78	49.1%	8	38.1%	86		
	41-50	40	25.2%	6	28.6%	46		
	> 50	22	13.8%	6	28.6%	28		
Total		159	100.0%	21	100.0%	180		

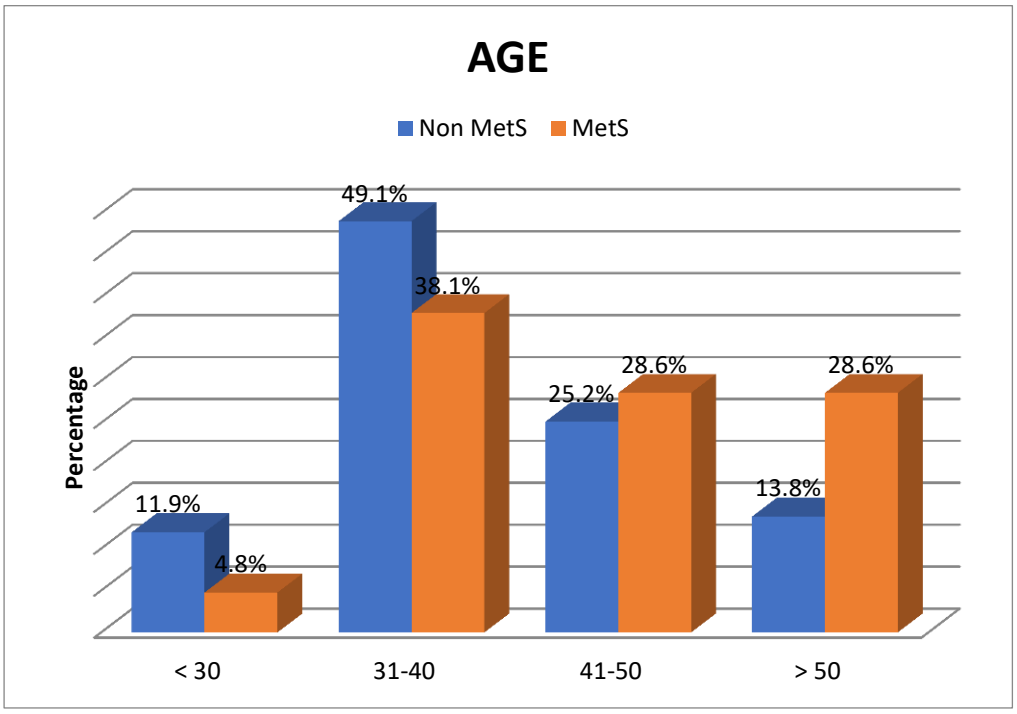

Figure 12: Bar diagram showing age distribution of study participants between non-metabolic syndrome and metabolic syndrome group.

Table 14: Mean age distribution of study participants between non-metabolic syndrome and metabolic syndrome group.

	Non MetS		MetS		Z	p-value
	Mean	**SD**	**Mean**	**SD**		
Age(years)	45.63	12.79	51.14	11.29	-1.880	0.062

The mean age group of Non MetS group patients was 45.63 ± 12.79 years and in MetS group was 51.14 ± 11.29 years. Age group between two groups was comparable and was statistically insignificant (p value > 0.05).

Table 15: BMI distribution of study participants between non-metabolic syndrome and metabolic syndrome group.

		Group				Total	Chi-square value	p-value
		Non MetS	Non MetS	Met S	MetS			
BMI(Kg/m2)	< 18.5	9	5.6%	0	0.0%	9	33.477	0.001
	18.6-24.9	86	54.1%	0	0.0%	86		
	25-29.9	34	21.4%	6	28.6%	40		
	> 30	30	18.9%	15	71.4%	45		
Total		159	100%	21	100.0%	180		

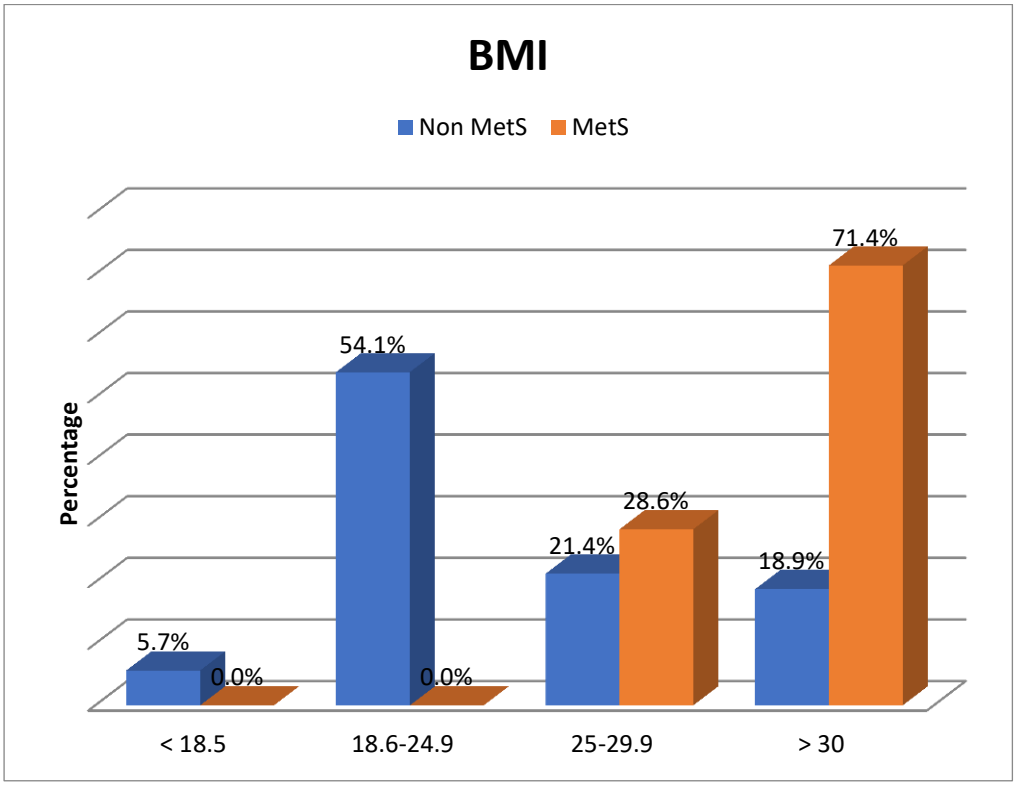

Figure 13: Bar diagram showing BMI distribution of study participants between non-metabolic syndrome and metabolic syndrome group.

Table 16: Mean BMI distribution of study participants between non-metabolic syndrome and metabolic syndrome group.

	Non MetS		MetS		Z	p-value
	Mean	**SD**	**Mean**	**SD**		
BMI(Kg/m2)	23.97	4.68	30.54	1.97	-6.345	0.001

Out of 180 patients, 64patients (40.3%) in non-MetS group and 21 patients (100%) in MetS group had BMI>=25kg/m2. Mean BMI of MetS group and non-MetS group was 30.54 ± 1.97 and 23.97 ± 4.68 kg/m2 and was statistically significant (p value<0.05) higher in MetS group patients.

Table 17: Waist circumference component distribution of study participants between non-metabolic syndrome and metabolic syndrome group.

		Group				Total	Chi-square value	p-value
		Non MetS		MetS				
Waist Circumference(cm)	male>=90cm, female>=80 cm	36	22.6%	21	100%	57	51.301	0.0001
	male<90cm, female<80 cm	123	77.4%	0	0.0%	123		
Total		159	100%	21	100%	180		

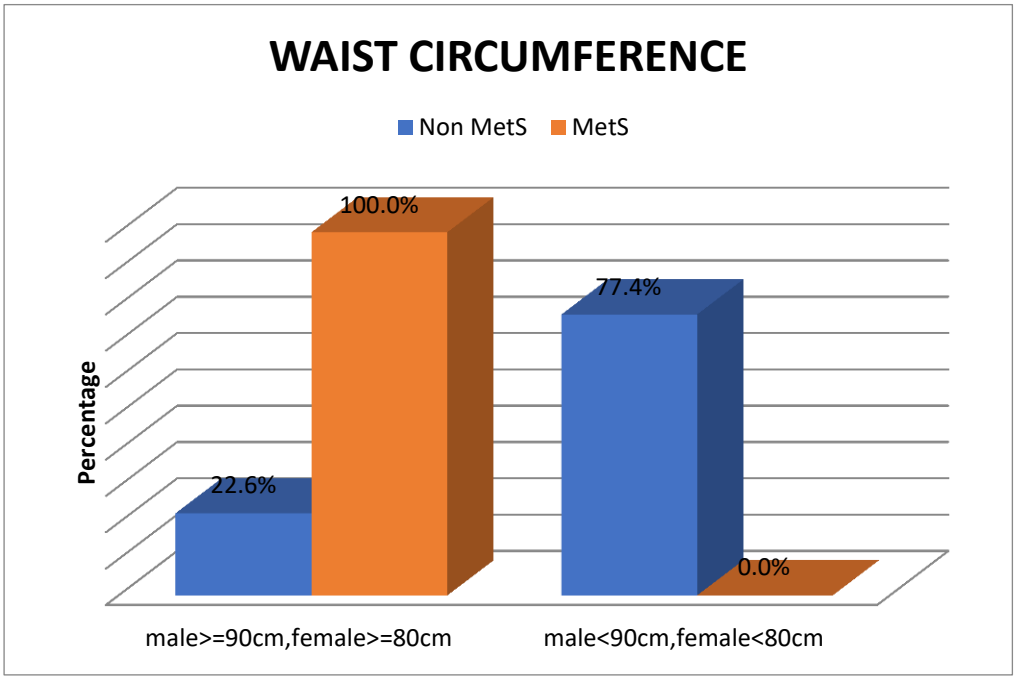

Figure 14: Bar diagram showing Waist circumference component distribution of study participants between non-metabolic syndrome and metabolic syndrome group.

Table 18: Mean waist circumference component distribution of study participants between non-metabolic syndrome and metabolic syndrome group.

	Non MetS		MetS		Z	p-value
	Mean	**SD**	**Mean**	**SD**		
Waist Circumference (cm)	83.11	11.34	99.81	6.45	-6.599	0.001

The waist circumference component according to IDF criteria accounts to 22.6% (36 patients) in non-MetS group and 100% (21 patients) in MetS group and was tested for significance and component was statistically significant (p value<0.05). Mean waist circumference in MetS and non-MetS group was 99.81±6.45 and 83.11±11.34 cm respectively and was statistically significant (p value<0.05) higher in metabolic syndrome patients.

Table 19: Blood pressure component distribution of study participants between non-metabolic syndrome and metabolic syndrome group.

		Group				Total	chi-square value	p-value
		Non MetS		MetS				
Blood Pressure	SBP>=130 or DBP>=85mmHg or on treatment	65	40.9%	16	76.2%	81	9.345	0.002
	SBP<130 or DBP<85mmHg	94	59.1%	5	23.8%	99		
Total		159	100%	21	100%	180		

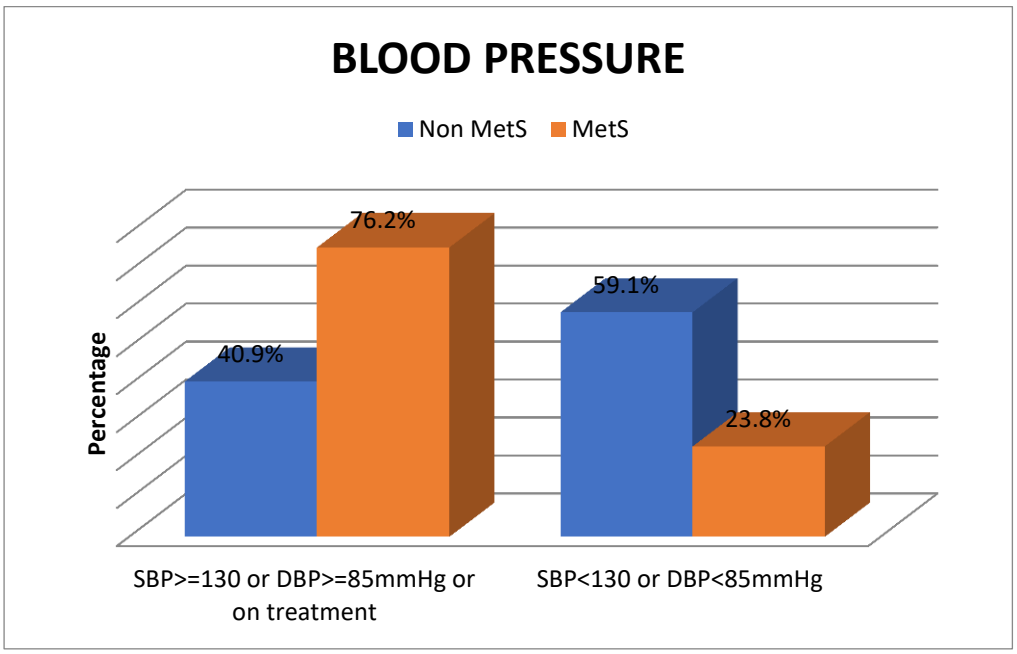

Figure 15: Bar diagram showing Blood pressure component distribution of study participants between non-metabolic syndrome and metabolic syndrome group.

Table 20: Mean Blood pressure component distribution of study participants between non-metabolic syndrome and metabolic syndrome group.

	Non MetS		MetS		Z	p-value
	Mean	**SD**	**Mean**	**SD**		
Systolic Blood Pressure(mmHg)	124.87	16.57	137.81	15.64	-3.384	0.001
Diastolic Blood Pressure(mmHg)	79.14	11.33	88.00	9.40	-3.428	0.001

The Blood Pressure component according to IDF criteria accounts to 40.9% (65 patients) in non-MetS group and 76.2% (16 patients) in MetS group and was tested for significance and component was statistically significant (p value<0.05). Mean SBP in MetS and non-MetS group was 137.81±15.64 and 124.87±16.57 mmHg respectively and was statistically significant (p value<0.05) higher in metabolic syndrome patients. Similarly Mean DBP in MetS and non-MetS group was 88.00±9.40 and 79.14±11.33 mmHg respectively and was statistically significant (p value<0.05) higher in metabolic syndrome patients.

Table 21: Fasting blood sugar component distribution of study participants between non-metabolic syndrome and metabolic syndrome group.

		group				Total	chi-square value	p-value
		Non MetS		MetS				
Fasting blood sugar	>=100mg/dl or on treatment	51	32.1%	19	90.5%	70	26.622	0.001
	<100mg/dl	108	67.9%	2	9.5%	110		
Total		159	100%	21	100%	180		

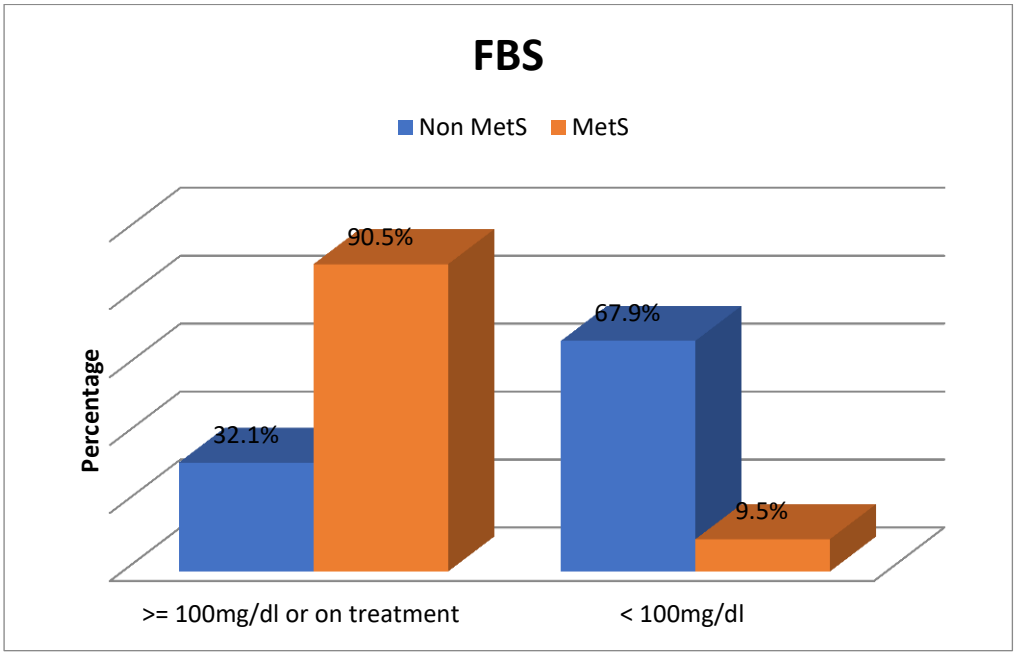

Figure 16: Bar diagram showing FBS component distribution of study participants between non-metabolic syndrome and metabolic syndrome group.

Table 22: Mean Fasting blood sugar component distribution of study participants between non-metabolic syndrome and metabolic syndrome group.

	Non MetS		MetS		Z	p-value
	Mean	**SD**	**Mean**	**SD**		
Fasting Blood Sugar(mg/dl)	99.85	32.04	148.24	44.50	-6.189	0.001

The Fasting blood sugar component according to IDF criteria accounts to 32.1% (51 patients) in non-MetS group and 90.5% (19 patients) in MetS group and was tested for significance and component was statistically significant (p value<0.05). Mean FBS in MetS and non-MetS group was 148.24±44.50 and 99.85±32.04 mg/dl respectively and was statistically significant (p value<0.05) higher in metabolic syndrome patients.

Table 23: Triglycerides component distribution of study participants between non-metabolic syndrome and metabolic syndrome group.

		group				Total	chi-square value	p-value
		Non MetS		MetS				
Triglycerides	>=150 mg/dl or on specific treatment for lipid abnormality	33	20.8%	17	81.0%	50	33.507	0.001
	< 150mg/dl	126	79.2%	4	19.0%	130		
Total		159	100%	21	100%	180		

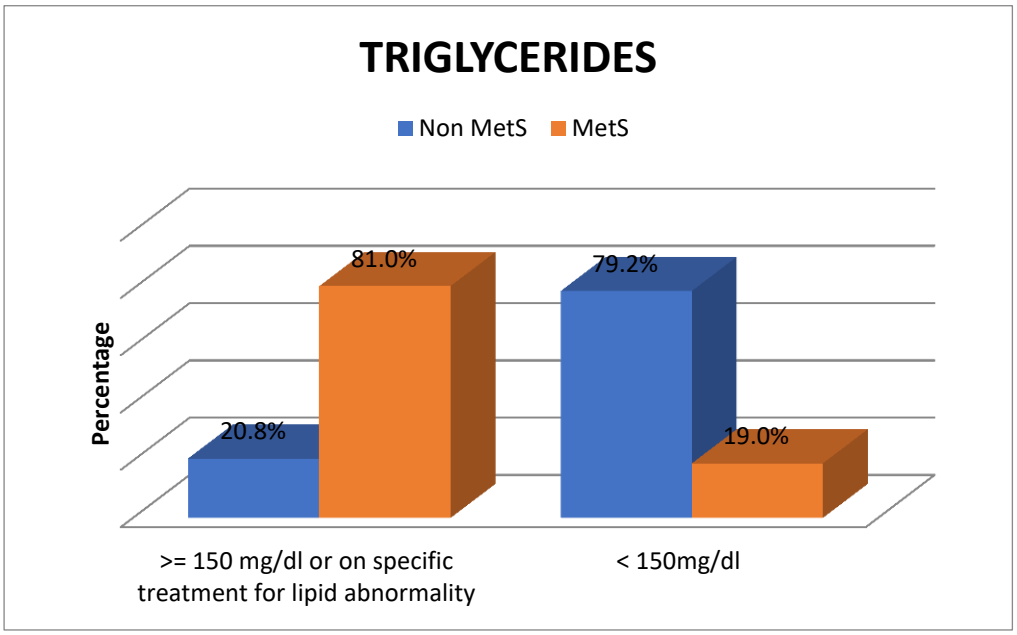

Figure 17: Bar diagram showing Triglycerides component distribution of study participants between non-metabolic syndrome and metabolic syndrome group.

Table 24: Mean Triglycerides component distribution of study participants between non-metabolic syndrome and metabolic syndrome group.

	Non MetS		MetS		Z	p-value
	Mean	**SD**	**Mean**	**SD**		
Triglycerides (mg/dl)	136.09	28.40	176.90	30.80	-6.128	0.001

The Triglycerides component according to IDF criteria accounts to 20.8 % (33 patients) in non-MetS group and 81.0% (17 patients) in MetS group and was tested for significance and component was statistically significant (p value<0.05). Mean Triglycerides in MetS and non-MetS group was 176.90±30.80 and 136.09±28.40 mg/dl respectively and was statistically significant (p value<0.05) higher in metabolic syndrome patients.

Table 25: HDL component distribution of study participants between non-metabolic syndrome and metabolic syndrome group.

		group				Total	chi-square value	p-value
		Non MetS		MetS				
HDL	males<40 mg/dl, female < 50mg/dl or on specific treatment for lipid abnormality	33	20.8%	13	61.9%	46	16.511	0.001
	males>=40 mg/dl, female >=50mg/dl	126	79.2%	8	38.1%	134		
Total		159	100%	21	100%	180		

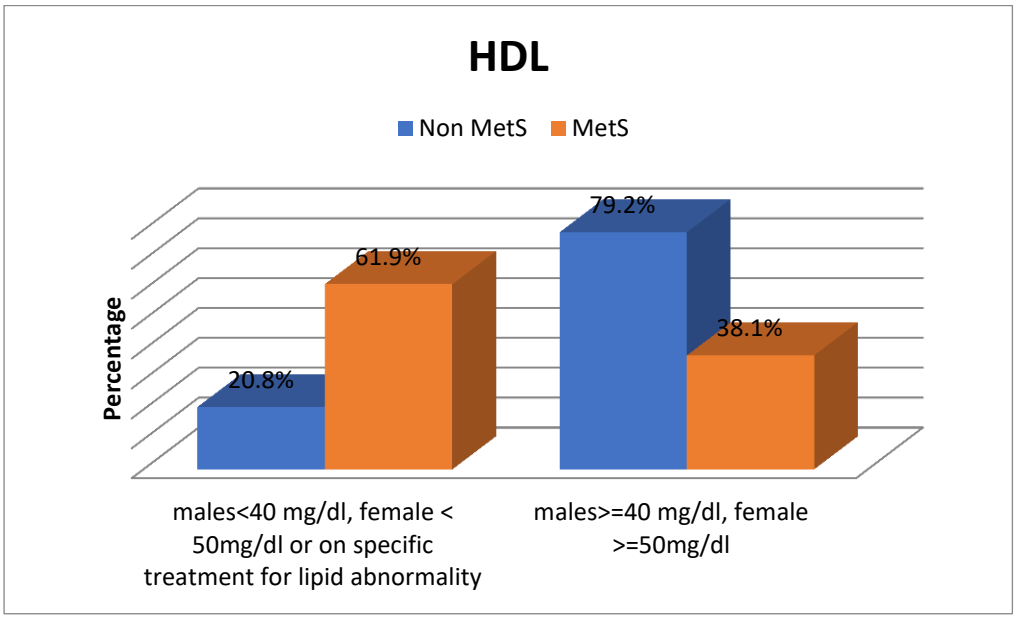

Figure 18: Bar diagram showing HDL component distribution of study participants between non-metabolic syndrome and metabolic syndrome group.

Table 26: Mean HDL component distribution of study participants between non-metabolic syndrome and metabolic syndrome group.

	Non MetS		**MetS**		**Z**	**p-value**
	Mean	SD	Mean	SD		
HDL (mg/dl)	51.95	10.28	44.33	13.04	3.087	0.002

The HDL component according to IDF criteria accounts to 20.8 % (33 patients) in non-MetS group and 61.9% (13 patients) in MetS group and was tested for significance and component was statistically significant (p value<0.05). Mean HDL in MetS and non-MetS group was 44.33±13.04 and 51.95±10.28 mg/dl respectively and was statistically significant (p value<0.05) Lower in metabolic syndrome patient.

Table 27: Stone composition of Metabolic syndrome group of patients.

Stone Composition	Frequency	Percent
Calcium oxalate	6	33.35%
Calcium phosphate	1	5.55%
Uric acid	8	44.44%
Magnesium ammonium	3	16.66%
Others	0	0%
Total	18	100

Stones of 18 out of 21 patients was sent for analysis in our institution, 3 samples of stones were not retrieved for analysis. Uric acid stones, calcium oxalate stones, magnesium ammonium and calcium phosphate stones were component in 8(44.44%), 6(33.35%), 3(16.66%) and 1(5.55%) respectively.

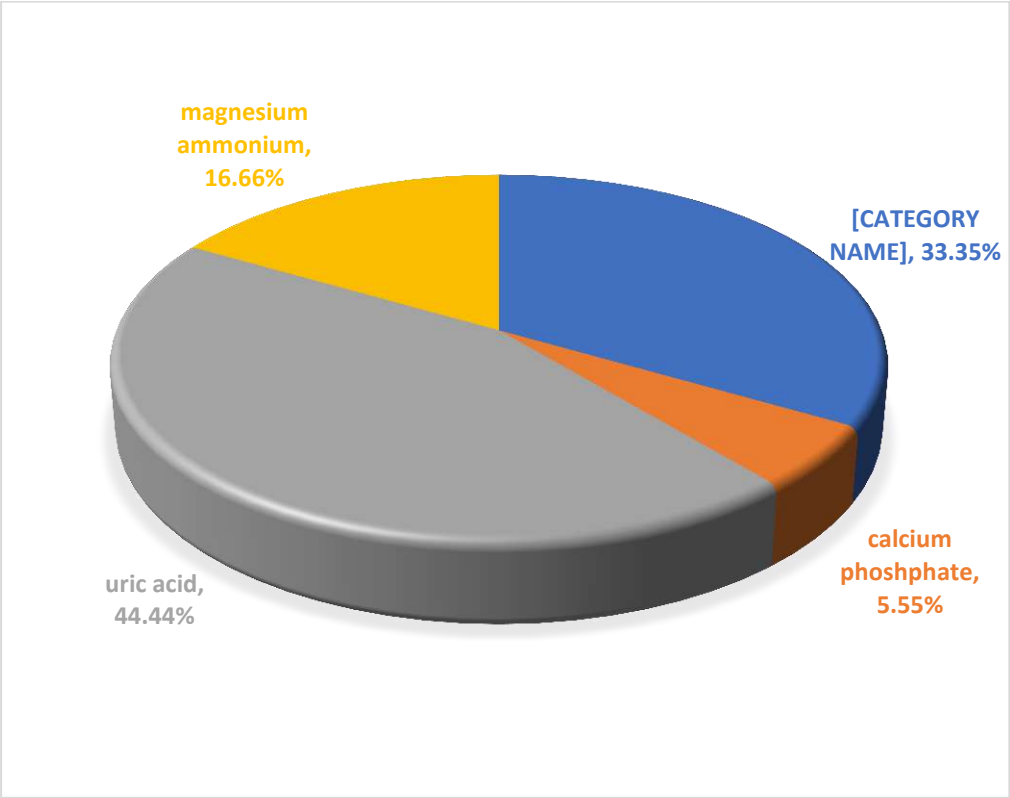

Figure 19: Pie chart showing Stone composition distribution of metabolic syndrome group of patients.

Table 28: Stone composition distribution in metabolic syndrome patients

		Calcium oxalate		Calcium phosphate		Magnesium phosphate		Uric acid		Total
		No. of cases	%	No. of cases	%	No. of cases	%	No. of cases	%	
Age group (years)	< 30	0	0.0%	0	0.0%	1	33.3%	0	0.0%	1
	31-40	1	16.7%	1	100.0%	1	33.3%	4	50.0%	7
	41-50	3	50.0%	0	0.0%	1	33.3%	1	12.5%	5
	> 50	2	33.3%	0	0.0%	0	0.0%	3	37.5%	5
Sex	F	1	16.7%	0	0.0%	2	66.7%	5	62.5%	8
	M	5	83.3%	1	100.0%	1	33.3%	3	37.5%	10
BMI (kg/m2)	< 18.5	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0
	18.6-24.9	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0
	25-29.9	0	0.0%	0	0.0%	2	66.7%	2	25.0%	4
	> 30	6	100.0%	1	100.0%	1	33.3%	6	75.0%	14
Waist Circumference	male>=90cm, female>=80cm	6	100.0%	1	100.0%	3	100.0%	8	100.0%	18
	male<90cm, female<80cm	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0

Blood Pressure	SBP>=130 or DBP>=85mmHg or on treatment	5	83.3%	1	100.0%	3	100.0%	6	75.0%	15
	SBP<130 or DBP<85mmHg	1	16.7%	0	0.0%	0	0.0%	2	25.0%	3
FBS	>= 100mg/dl or on treatment	5	83.3%	1	100.0%	3	100.0%	8	100.0%	17
	< 100mg/dl	1	16.7%	0	0.0%	0	0.0%	0	0.0%	1
TGL	>= 150 mg/dl or on specific treatment for lipid abnormality	6	100.0%	1	100.0%	2	66.7%	5	62.5%	14
	< 150mg/dl	0	0.0%	0	0.0%	1	33.3%	3	37.5%	4
HDL	males<40 mg/dl, female < 50mg/dl or on specific treatment for lipid abnormality	3	50.0%	1	100.0%	0	0.0%	4	50.0%	8
	males>=40 mg/dl, female >=50mg/dl	3	50.0%	0	0.0%	3	100.0%	4	50.0%	10
Total		6	100.0%	1	100.0%	3	100.0%	8	100.0%	18

In MetS group, 18 out of 21 patient stones were sent for analysis in our study, Calcium oxalate stones were common in male gender (5 out of 6 patients) whereas uric acid stones in female gender (5 out of 8 patients)

8 (100%) of uric acid stones were associated with FBS component, 6 (75%) with BP component, 5 (62.5%) with TGL component and 4 (50%) with HDL component.

5 (83.3%) of calcium oxalate stones were associated with FBS and BP component, 6 (100%) with TGL component and 3 (50%) with HDL component

DISCUSSION

Urolithiasis is a common disorder affecting urinary system. The morbidity due to stone disease and the huge amount spend on diagnosis, treatment and follow up leads to search for preventive strategies in urolithiasis.

Historically, stone disease affected adult men more commonly than adult women. By a variety of indicators, including inpatient admissions, outpatient office visits, and emergency department visits, men were affected two to three times more often than women [55, 56]. However, recent evidence suggests that the difference in incidence between men and women is decreasing. Scales and colleagues [57] found that, discharges for women increased by 17% while discharges for men decreased by 8.1%. This trend reflects a change in the ratio of male-to-female discharges from 1.7 in 1997 to 1.3 in 2002.

In an analysis of data from 268,553 patients, Pietro Manuel Ferraro and colleagues [58] found that the risk of kidney stones was constantly higher among men across age categories. After age modification, men still had a significant 2.3-fold higher risk for kidney stones compared with women. Prior to 1990, men had a significant 2.7-fold higher risk for kidney stones compared with women, whereas from 2010 onward, men had a significant 1.7-fold higher risk. Stone occurrence is relatively uncommon before age 20 but peaks in incidence in the fourth to sixth decades of life [59]. Ahmad and associates [60] concluded that highest prevalence of the renal calculus disease was in the age group 40-49 in males and in the age group 30-39 in females.

Safdar and colleagues [61] concluded that the median age at diagnosis was 29 years and the mean age at diagnosis was 36.91 years (SD = 18.66, Range of 20–99). Two peaks of age were observed, the first peak was at the 21 to 25 years age group representing 34.4% of the kidney stones patients. The second peak was older than 47 years.

In our study of 180 patients also, male patients were affected more than female counterpart which was 129 (71.7%) and 51 (28.3%) patients respectively. Minimum age of subject was 19 years and

maximum age was 75 years. Maximum of our patients fall in range of 31 to 50 years of range which accounts to 132 (73.3%) patients. Mean age of our study was 46.27±12.72 years.

The aim of the present study was to determine the association between MetS components and incidence of Urolithiasis. Metabolic syndrome and Urolithiasis Studies of large patient cohorts have established the correlation with MetS and the development of kidney stones A systematic review and meta-analysis by Besiroglu et al. confirmed the strong association of metabolic syndrome with urolithiasis with a 1.4-fold increase [62]. West and associates analysed the United States National Health and Nutrition Examination Survey (NHANES III) and institute that patients with MetS had two times the risk of developing a kidney stone based on self-reporting [63]. West and associates [63] stated that the kidney stone prevalence was 3.7% with no traits, 7.5% for three traits, and 9.8% for five traits. Similar associations have been reported in Japan and South Korea. This relationship has also been demonstrated in radiographic screening studies. Jeong and colleagues [64] reported that among almost 34895 residents of South Korea who were screened with ultrasonography or CT, 2.4% had stones, 13.7% had MetS, and the odds ratio based on imaging for MetS and kidney stones was 1.25. Rendina et al [65]. Also reported that MetS was significantly associated with ultrasonographic evidence of nephrolithiasis.

In our study, 21(11.7%) patients diagnosed to have metabolic syndrome according to IDF criteria, prevalence of stone in patient of metabolic syndrome in our study matches with previous studies. Male to female ratio in non-MetS group was 2.8:1 whereas in MetS group was 1.3:1 which was considerably lower and signifies the incidence of stone disease is more in metabolic syndrome female compare to non-metabolic patients. Mean age of MetS patient was 51.14 ± 11.29 years and non-MetS patient was 45.63 ± 12.79 years, which was not statistically significant with p value of 0.062.

The key parameters depicting metabolic syndrome include overweight, arterial hypertension and disturbances of the carbohydrate metabolism.

However, the link between urolithiasis and metabolic syndrome has suggested a possible role of multiple metabolic risk factors in the development of urolithiasis [66]. Waist circumference is a fast metric of visceral obesity. The accretion of adipose tissue increases release of adipocyte derived inflammatory cytokines which potentiate other factors contributing to MetS [67]. Taylor and associates [68] utilized three large epidemiological prospective cohort studies to examine 4827 kidney stone incidents. They displayed that body mass index (BMI) and waist circumference, two distinct measures of obesity, were associated with an amplified risk of kidney stone formation. Inci and associates [69] institute BMI to be significantly higher in stone forming patients.

In a study of 84 225 women with no history of kidney stones, Sorensen and colleagues [70] identified a BMI dependent increased risk of incident kidney stones, 25 to 29.9 kg/m2 (1.3-fold), 30 to 34.9 kg/m2 (1.62-fold), and >35 kg/m2 (1.81-fold) as compared to BMI < 25 kg/m2. An increased incidence of urolithiasis of up to 75% has been seen in patients who are overweight and obese [71].

Body fat may influence kidney stone development. Growing visceral adipose tissue, as measured by computed tomography (CT), was described to be associated with the hazard of developing uric acid and calcium oxalate stones in kidney [72]. Renal stone risk has also been known to be positively correlated with the ratio of visceral to subcutaneous fat tissue and non-alcoholic fatty liver disease.

In our study, BMI of patient, as per Asian guidelines, in MetS group (21 patient) was above >25 kg/m2 in all patient and out of which 15 (71.4%) patients were obese with BMI >= 30 kg/m2 and was statistically significant with p value of 0.001 compare to non-MetS group of patients. Mean BMI of patients in MetS and non-MetS group was 30.54 ± 1.97 and 23.97 ± 4.68 kg/m2 respectively and was statistically significant with p value of 0.001. Mean waist circumference was 99.81 ± 6.45 and 83.11 ± 11.34 cm in MetS and non-MetS group respectively and was significant statistically with p value of 0.001. Hence our study shows obesity component was a significant risk factor for urolithiasis in patient with metabolic syndrome.

Dyslipidaemia and nephrolithiasis Raised serum triglycerides and low high-density lipoprotein (HDL) levels, components of MetS, negatively impact cardiovascular health. Dyslipidaemia has been proposed as an independent risk factor for nephrolithiasis as it is associated with lower urine Ph [73]. Masterson and colleagues [74] in a retrospective study of 52,184 patients proved an association between dyslipidaemia and nephrolithiasis, hazard ratio of 2.2. While low-density lipoprotein (LDL) and triglycerides were not independently associated with stone formation, low HDL value had a hazard ratio of 1.4.

A total of 50 patients (27.8%) in our study had the Triglycerides component according to IDF criteria, which accounts to 20.8 % (33 patients) in non-MetS group and 81.0% (17 patients) in MetS group and was tested for significance and component was statistically significant (p value<0.05). Mean Triglycerides in MetS and non-MetS group was 176.90±30.8 0 and 136.09±28.40 mg/dl respectively and was statistically significant (p value<0.05) higher in metabolic syndrome patients. A total of 46 patients (25.6%) had HDL component according to IDF criteria, which accounts to 20.8 % (33 patients) in non-MetS group and 61.9% (13 patients) in MetS group and was tested for significance and component was statistically significant (p value<0.05). Mean HDL in MetS and non-MetS group was 44.33 ± 13.04 and 51.95 ± 10.28 mg/dl respectively and was statistically significant (p value<0.05) Lower in metabolic syndrome patients. We concluded from our study also that both raised TG and lower HDL as a component of metabolic syndrome was a significant risk factor for formation of stones in MetS patient compared to non-Mets patients.

Hypertension, a component of MetS, has a bidirectional association with kidney stone risk. Patients with hypertension have been reported to hold a higher risk for stone development and stone formers are liable to develop hypertension compared to the general population [75, 76].Shang and colleagues[77] in a meta-analysis observational studies demonstrated total of 7 articles including 9 studies (n = 313,222 participants) were eventually identified in this meta-analysis. In comparison with the patients who did not have nephrolithiasis,

nephrolithiasis significantly increased the risk of hypertension (OR, 1.43; 95% CI, 1.30–1.56), with significant heterogeneity between these studies (I 2 = 83.5%, P <0.001.

A total of 81 patients (45%) in our study had Blood Pressure component according to IDF criteria, which accounts to 40.9% (65 patients) in non-MetS group and 76.2% (16 patients) and was tested for significance and component was statistically significant (p value<0.05). Mean SBP in MetS and non-MetS group was 137.81 ± 15.64 and 124.87 ± 16.57 mmHg respectively and was statistically significant (p value<0.05) higher in metabolic syndrome patients Similarly Mean DBP in MetS and non-MetS group was 88.00 ± 9.40 and 79.14 ± 11.33 mmHg respectively and was statistically significant (p value<0.05) higher in metabolic syndrome patients. Hence our study concluded that hypertension as a component in metabolic syndrome patient was a significant risk factor for formation of stones in MetS patients.

In three large cohorts, type 2 Diabetes Mellitus was a risk factor for developing kidney stones; on multivariate analysis, Taylor et al. study reported increased risk of stone diseases in diabetes patients. The relative risk of stone disease in those with diabetes was 1.38 in older women, 1.67 in younger women, and 1.31 in men [78]. Uric acid kidney stone formation has been linked to diabetes. Insulin resistance has been correlated to the reduction in renal ammonium production and low urinary pH, resulting into formation of urolithiasis [79]. A study by Pak et al. concluded that stone-forming patients with diabetes mellitus have a high prevalence of uric acid stones [80]. Fasting glucose levels assist in detecting insulin resistant diabetes mellitus, a disease with progressive negative systemic effects. Hyperglycaemia secondary to insulin resistance leads to accumulation of advanced glycation end products (AGEs) inducing a pro-inflammatory state and vascular endothelial dysfunction [81]. Moreover, direct correlation between low urinary pH and number of metabolic syndrome risk factors as well as inverse correlation between degree of insulin resistance and urinary pH have been shown in a cross-sectional study performed by Maalouf et al [82].

A total of 70 patients (38.9%) in our study had Fasting blood sugar component according to IDF criteria, which accounts to 32.1% (51 patients) in non-MetS group and 90.5% (19 patients) in MetS group and was tested for significance and component was statistically significant (p value<0.05). Mean FBS in MetS and non-MetS group was 148.24 ± 44.50 and 99.85 ± 32.04 mg/dl respectively and was statistically significant (p value<0.05) higher in metabolic syndrome patients. Hence our study shows Fasting blood sugar as a component of metabolic syndrome was a significant risk factor in formation of stones in MetS patients compared to non-MetS patients.

A study by Maalouf et al. stated that increased uric acid excretion appears to be commonly related to insulin resistance, which further relates with obesity [83]. Zhang et al. study concluded that hyperuricemia is an independent risk factor of metabolic syndrome [84]. Other previous studies have also shown that individuals with high uric acid levels have 1.6 times higher odds of developing metabolic syndrome. The mechanism involved in this association may include reduction in endothelial nitric oxide bioavailability by uric acid or hyperinsulinemia reduces urinary uric acid excretion by the effect of insulin on urinary tubules leading to hyperuricemia [85-87].

Pedro Valente and colleagues [88] did Observational and retrospective study of all urinary calculi analysis came to result that Patients with metabolic syndrome presented a higher proportion of uric acid calculi (66.1% vs. 0%, p <0.001) and ammonium urate calculi (38.7% vs. 17%, p = 0.001). Patients without metabolic syndrome had a higher proportion of calcium oxalate calculi (58.8% vs. 24.2%, p <0.001) and calcium phosphate (46.7% vs. 19.4%, p <0.001).

Patients with MetS typically harbour calcium oxalate and uric acid stones. Kadlec and associates [89] analysed nearly 600 patients for the involvement of MetS on kidney stone composition. They found that calcium oxalate stones were the most prevalent and uric acid was the next most common composition. Calcium phosphate stones were less prevalent. Relative to the generic stone forming population, the per-centage of uric acid stones was significantly higher, and the percentage

of calcium phosphate stones was significantly lower in patients with MetS.

In our study stones of 18 out of 21 patients in MetS group was sent for biochemical stone analysis and Uric acid stones, calcium oxalate stones, magnesium ammonium and calcium phosphate stones were component in 8 (44.44%), 6 (33.35%), 3 (16.66%) and 1 (5.55%) respectively. So, this study concluded that uric acid stones incidence was higher in metabolic syndrome patients and our results were comparable to previous studies done.

In our study, Calcium oxalate stones were common in male gender (5 out of 6 patients) whereas uric acid stones in female gender (5 out of 8 patients). From our study, we can conclude that MetS female was at more risk at formation of uric acid stones than MetS male.100% of uric acid stones in MetS group were associated with FBS component in our study, this signifies the association of insulin resistance with uric acid stones. Calcium oxalate stones in MetS group were also associated with TG (100%), FBS and BP (83.3% each) and HDL component (50%) of metabolic syndrome, which again signifies risk of calcium oxalate stones with metabolic syndrome component.

SUMMARY & CONCLUSION

This study was conducted to evaluate the association of metabolic syndrome in urolithiasis patient population in our part of country. Our study observations suggest that metabolic components which includes hypertension, diabetes mellitus, hypertriglyceridemia, and reduced HDL were significantly associated with the increased risk of developing stones in a patient of metabolic syndrome. Therefore, presence of metabolic syndrome and its components are significantly associated with urolithiasis in Indian patients. In our study a total of 21 patients were suffering from MetS according to IDF criteria which is 11.6 % of patients with urolithiasis included in our study. These results are corroborative with previous studies. Male to female ratio in non-MetS group was 2.8:1 whereas in MetS group was 1.3:1 which was considerably lower and signifies the incidence of stone disease is more in metabolic syndrome female compare to non-metabolic patients.

In our study we have sent stones of 18 patients with metabolic syndrome for analysis and 44% of patients have uric acid stones. Calcium oxalate stones were common in male gender (83.3%) whereas uric acid stones in female gender (62.5%). 100% of uric acid stones were associated with FBS component in our study, this signifies the association of insulin resistance with uric acid stones and increase risk of uric acid stones in metabolic syndrome patient.

Due to globalization of economy and increased availability of easy life style commodities there is increased prevalence of metabolic syndrome in our community. Medical management is directed at correcting the underlying metabolic abnormalities of metabolic syndrome as well as those that lead to stone formation. Lifestyle and diet modification is the primary approach independent of risk factors. Patients should be encouraged to exercise regularly, lose weight to achieve a BMI of less than 25kg/m2 and manage conditions that lead to excessive fluid loss. Adequate fluid intake, in order to produce a diuresis of at least 2 L/day is pivotal to stone prevention for all stone formers. Appropriate lifestyle and dietary modifications should never be

abandoned even when a pharmacological method is started. The Mediterranean diet stresses consumption of olive oil, fruits, vegetables, and seeds, which contain mono- and poly- unsaturated fatty acids, dietary fibre, magnesium, potassium, antioxidant vitamins (i.e., folate, vitamin E), polyphenols, and other phytochemicals that combat oxidative stress, inflammation, and insulin resistance. The positive effects of this diet have also been studied relative to lithogenic risk in metabolic syndrome patients and have been found to be significant. It is clear from our study that various component of metabolic syndrome is associated with risk of urolithiasis so it is important that patients with known diabetes and hypertension should have controlled sugar and blood pressure and should be educated about risk of stone formation in them and adequate preventive measures mentioned above.

We can also recommend from our study that patient with metabolic syndrome should also undergo biochemical evaluation for stone formation as these patients may have various biochemical abnormalities which can be corrected promptly and reduces the risk of stone formation. Patients with MetS has increase prevalence of uric acid stones compared to calcium oxalate stones in non-MetS patients. As Correction of low urine pH by urine alkalinization is central in preventing recurrent uric acid stones. Along with alkalinization, the addition of allopurinol is indicated in cases of hyperuricemia or hyperuricosuria (excretion >1.2 g/day). Allopurinol is a xanthine oxidase inhibitor that prevents uric acid production from purine. Febuxostat, a nonpurine inhibitor of xanthine oxidase has recently been shown to lower urinary uric acid.

Although definitive therapeutic recommendations must await further studies, it seems reasonable for the urologist, working with multidisciplinary team to recommend these important lifestyle modifications to the patient of urolithiasis with metabolic syndrome, along with currently accepted empirical treatments of stone disease.

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S.No.	MRD	Name	Sex	Age (Years)	Stone Location	BMI (kg/m2)	Waist Circumference (cm)	SBP (mmHg)	DBP (mmHg)	FBS (mg/dl)	TGL (mg/dl)	HDL (mg/dl)	Anti Hypertensive Medication	Anti diabetes Mellitus Medication	Lipid Lowering Agents
1	1200571	SK	F	42	L	32.1	103	140	100	110	146	56	Yes	Yes	No
2	1174794	GK	F	46	L	21.6	74	136	96	99	131	57	Yes	Yes	No
3	1193992	SB	F	60	R	25.7	60	116	82	86	134	61	No	No	No
4	786609	V	F	52	R	23.2	84	110	70	88	145	54	No	No	No
5	1160494	NK	F	50	L	26.1	71	130	90	97	190	52	Yes	No	No
6	1121390	VG	M	54	L	17.6	65	160	100	60	138	69	Yes	No	No
7	690722	KB	F	70	R	16.5	72	130	60	80	106	45	No	Yes	Yes
8	1257605	IK	F	61	R	29.5	96	120	80	205	120	46	Yes	Yes	Yes
9	188456	M	M	70	L	32.1	103	160	90	89	176	35	No	Yes	Yes
10	1265693	RR	M	57	R	31.5	110	120	80	160	210	30	Yes	Yes	Yes
11	1267607	SR	F	42	L	23.2	76	138	90	106	166	51	Yes	Yes	Yes
12	30509	M	F	60	R	25.2	79	140	100	110	140	40	Yes	Yes	No
13	1220451	ON	M	66	R	30.1	94	120	70	94	225	26	Yes	No	Yes
14	1207763	M	F	20	R	19.1	74	138	98	94	100	49	Yes	No	No
15	1210406	KK	F	54	R	30.1	89	110	70	89	120	51	Yes	No	No
16	1248808	NK	F	39	R	26.6	81	150	70	60	130	54	Yes	No	No
17	401014	S	M	30	R	21.9	88	110	70	110	120	49	No	Yes	No
18	1271272	V	M	23	R	20.6	80	110	60	70	121	47	No	No	No
19	1262627	SS	M	30	R	19.6	84	100	60	96	171	44	No	No	Yes
20	1013614	SK	F	36	R	30.5	82	124	80	112	110	61	No	Yes	No
21	1260008	IN	M	42	L	21.8	84	100	70	109	96	46	No	No	No
22	1257032	US	M	21	R	25.5	83	110	70	84	130	45	No	No	No
23	49466	RK	M	50	L	31.2	109	110	70	95	112	52	Yes	No	No
24	1219671	MK	F	47	R	23.6	78	156	80	90	165	30	Yes	No	No
25	1286868	AK	M	43	L	20.6	84	110	80	85	125	57	No	No	No
26	1288163	S	M	65	R	21.7	86	110	70	167	131	55	Yes	Yes	No
27	1287424	MD	F	36	L	19.2	66	142	86	91	134	69	Yes	Yes	No
28	1152615	MR	F	50	R	31.5	104	160	94	192	190	60	Yes	Yes	Yes
29	1275182	BD	F	65	R	32.2	105	150	80	210	140	25	No	Yes	Yes
30	397299	A	M	41	R	17.6	76	120	84	70	110	51	No	No	No
31	1010641	UR	F	52	R	19.2	64	140	90	129	117	56	Yes	Yes	No
32	1264831	JS	M	50	R	32.5	120	128	80	50	142	48	No	No	No
33	1277740	SK	F	40	B/L	21.9	70	140	110	89	130	79	Yes	No	No
34	1277349	SR	F	46	R	20.6	72	100	60	63	128	51	No	No	No
35	1258524	NG	M	28	R	19.7	76	120	80	96	133	49	No	No	No
36	1275370	KS	M	38	L	21.7	72	110	70	76	161	51	No	No	No
37	1282771	CP	M	59	L	26.6	96	120	80	60	141	49	Yes	No	No

38	1282259	S	M	57	VESICAL	30.2	99	130	100	210	236	32	No	Yes	Yes
39	1262361	KS	M	35	B/L	31.8	120	110	70	180	132	51	No	Yes	No
40	1147820	BK	M	35	L	19.6	72	150	100	79	110	63	Yes	No	No
41	392986	K	F	36	B/L	26.9	87	150	100	210	180	61	Yes	Yes	No
42	1370054	NK	F	34	B/L	17.1	66	110	70	60	96	54	No	No	No
43	1360405	RG	F	46	R	29.2	97	120	82	130	200	54	No	Yes	No
44	1372666	GS	M	37	L	19.6	76	140	100	98	130	54	Yes	No	No
45	445824	KK	M	36	R	27.7	96	140	70	90	131	52	Yes	No	No
46	141370	MRG	M	51	L	25.6	82	138	70	104	129	51	Yes	No	No
47	1370187	RL	M	47	L	18.6	83	110	80	92	126	46	No	Yes	No
48	623114	AKJ	M	56	R	17.6	86	120	80	170	138	52	No	Yes	No
49	1365447	YK	M	65	L	20.6	96	128	90	61	139	59	Yes	No	No
50	1339035	YP	M	36	R	30.4	97	140	96	119	180	59	Yes	No	No
51	1247066	ND	F	70	R	31.5	88	140	80	94	124	56	Yes	No	No
52	1328544	JS	M	64	R	32.7	108	130	80	120	196	65	No	Yes	Yes
53	1342082	RS	M	36	R	21.6	81	130	100	116	266	57	No	Yes	Yes
54	1337756	VK	M	46	R	32.1	100	128	100	70	106	45	No	No	No
55	267515	JS	F	30	L	31.6	96	130	80	186	192	52	Yes	Yes	No
56	1367646	FS	M	45	R	30.6	103	154	96	160	148	54	No	Yes	No
57	1358702	MR	M	63	R	21.9	82	120	80	158	140	51	Yes	Yes	No
58	1361345	PS	M	37	B/L	22.9	84	110	80	120	99	52	No	Yes	No
59	1364513	AS	M	49	L	31.2	98	150	100	118	165	31	Yes	No	Yes
60	262302	AS	M	39	R	18.7	80	110	60	90	140	79	No	No	No
61	1383198	AS	M	32	L	19	82	120	80	84	132	56	No	No	No
62	1105575	JG	M	61	R	20.1	86	140	60	90	110	61	Yes	No	Yes
63	1385202	DS	M	44	R	21.6	77	100	60	120	131	41	No	No	No
64	1380883	UPS	M	43	L	30.5	79	160	110	101	112	54	Yes	No	No
65	1320244	SG	M	53	L	26.6	99	160	100	120	130	54	No	Yes	No
66	370849	AK	M	25	B/L	31.2	89	120	70	76	116	55	No	No	No
67	1346677	GS	M	46	R	30.6	88	110	70	100	101	41	No	No	No
68	1346476	GS	M	36	L	31.2	110	150	100	96	141	59	Yes	No	No
69	1350098	NK	M	48	L	21.6	82	120	80	140	130	43	No	Yes	No
70	1366346	MB	M	58	B/L	25	84	138	70	60	133	52	No	No	No
71	1126249	BH	F	33	L	21	70	110	70	96	132	67	No	No	No
72	1314649	GK	F	61	B/L	26.8	89	120	80	81	167	34	No	No	No
73	1520243	DK	M	37	R	33.8	101	150	90	210	199	31	Yes	Yes	Yes
74	1321863	HK	F	48	R	19	68	160	100	82	140	79	Yes	No	No
75	1335670	SP	M	54	B/L	17.6	62	150	80	101	124	36	Yes	No	No
76	1284916	SH	M	56	L	31.6	112	120	80	134	166	36	No	Yes	No
77	386065	BS	M	49	R	16.1	60	140	74	90	132	50	Yes	No	No

78	1315777	SK	M	46	B/L	21.6	80	120	80	94	136	44	No	No	No
79	1071512	R	F	39	R	25.8	78	110	70	99	189	41	No	No	Yes
80	204962	AO	M	42	R	26.2	86	110	80	90	134	50	No	No	No
81	187030	KU	F	43	R	31.9	103	150	90	140	149	51	Yes	Yes	No
82	1304206	RJ	M	50	R	28.9	92	120	80	115	200	39	No	No	No
83	1431462	US	M	21	R	30.6	76	110	70	70	120	66	No	No	No
84	1410230	SS	M	38	L	21.6	79	148	96	60	110	59	Yes	No	No
85	1388730	N	F	62	VESICAL	23.7	70	140	88	110	199	30	Yes	Yes	No
86	737025	LL	M	57	R	19.1	84	140	80	86	136	88	Yes	No	No
87	1408710	RK	M	45	L	18.7	76	140	90	60	120	50	Yes	No	Yes
88	1409682	HS	M	41	R	19.6	81	120	80	143	160	36	Yes	Yes	No
89	1409602	RP	M	47	L	19.7	76	140	82	105	149	32	Yes	Yes	No
90	1411016	KK	M	52	B/L	19.9	79	150	110	96	167	42	Yes	No	No
91	1389248	MK	F	50	L	26.7	77	130	60	78	131	52	No	No	No
92	141196	PS	M	48	R	33.7	100	110	70	76	210	42	No	No	No
93	1412224	R	M	73	R	27.1	87	136	80	165	155	30	Yes	Yes	No
94	1363145	SS	M	34	L	23.1	81	120	80	76	130	44	No	No	No
95	1290469	DR	F	51	L	31.8	89	124	80	99	148	43	No	No	No
96	1394456	R	M	54	L	20.1	86	100	70	150	125	49	No	Yes	No
97	1415033	SRS	M	63	B/L	20.7	85	110	60	118	134	53	No	Yes	No
98	1375956	GS	M	23	L	20.4	80	110	60	90	134	53	No	No	No
99	250068	SK	F	70	B/L	19.6	60	140	96	96	131	52	Yes	No	No
100	1416291	AG	M	40	R	23.6	86	140	70	90	96	52	No	No	No
101	1418602	JS	M	64	L	26.9	80	136	80	166	121	63	Yes	Yes	No
102	1422650	SS	M	52	L	26.8	84	140	80	97	132	51	Yes	No	No
103	1364546	JS	M	70	L	23.9	84	130	90	90	117	47	No	No	No
104	1372666	GS	M	59	R	30.4	89	110	76	70	86	49	No	No	No
105	1286563	SS	M	32	R	25.9	86	100	60	90	156	56	No	No	No
106	1359048	MS	M	34	R	31.8	84	110	80	98	149	27	No	No	No
107	1267607	SR	F	42	B/L	27.2	77	160	100	92	132	41	Yes	No	No
108	919923	SS	M	44	L	20.6	87	120	80	86	210	59	No	No	Yes
109	1376910	AS	M	24	L	29.5	80	120	80	80	116	42	No	No	No
110	1006586	JK	M	33	L	26.7	85	116	76	66	134	66	No	No	No
111	1380941	AK	F	36	L	20.8	70	110	70	98	111	55	No	No	No
112	267515	JM	F	30	R	19.6	69	136	94	97	134	57	Yes	No	No
113	298551	BM	M	58	VESICAL	19.9	84	110	70	170	120	49	No	Yes	No
114	1385936	SK	M	41	L	20.6	86	150	80	90	172	41	Yes	No	No
115	1383198	AS	M	32	L	31.6	108	110	70	188	149	45	No	Yes	No
116	1380883	UPS	M	43	L	33.2	100	120	80	187	111	70	No	Yes	No
117	1385282	SS	M	44	L	31.2	94	120	80	95	138	53	No	No	No

118	1383488	RS	M	35	R	30.8	94	128	90	69	130	55	No	No	No
119	1381064	MS	M	34	R	31.8	96	120	80	98	176	51	No	No	No
120	1333428	RS	M	61	R	19.1	82	160	80	95	111	50	Yes	No	No
121	1365447	YK	M	65	L	23.5	86	100	60	150	129	61	No	No	No
122	1388453	JK	F	45	R	23.6	79	120	70	114	110	67	No	Yes	No
123	1182570	TA	M	21	B/L	27.2	86	120	70	80	107	57	No	No	No
124	1392584	R	F	40	L	26.2	76	116	90	70	132	59	No	No	No
125	1352375	RPS	M	52	L	28.8	91	140	80	96	92	50	Yes	No	No
126	1396407	A	M	21	L	20.6	82	110	80	94	124	39	No	No	No
127	1401475	DO	M	50	R	19.6	74	130	80	86	120	46	No	No	No
128	684322	UK	M	42	R	20.6	83	90	60	66	110	45	No	No	No
129	801657	SK	M	60	L	20.7	84	130	70	130	140	41	No	Yes	No
130	1351130	GS	M	68	R	19.7	69	160	100	130	210	44	Yes	Yes	Yes
131	919923	SS	M	44	B/L	23.5	87	140	80	85	139	56	Yes	No	No
132	341802	CL	M	60	VESICAL	22.6	84	120	80	98	190	76	No	No	No
133	1295531	JK	F	75	R	21.7	76	120	80	85	180	55	No	No	Yes
134	1194120	GG	M	28	R	19	80	110	70	75	118	39	No	No	No
135	471954	ML	M	62	VESICAL	18.7	76	150	80	86	134	53	Yes	Yes	No
136	1313512	AS	M	51	L	19.6	80	120	70	120	110	71	No	No	No
137	1355805	UG	F	39	R	30.1	88	116	72	190	147	51	No	No	No
138	1359555	SL	M	49	L	32.8	101	140	90	90	130	66	Yes	No	No
139	1359628	TK	F	48	R	23.5	66	110	80	85	119	42	No	No	No
140	1290785	HS	M	57	L	29.3	92	140	90	86	134	52	Yes	No	No
141	1364513	AS	M	49	L	23.2	86	120	80	86	189	66	No	No	Yes
142	1320477	MS	M	33	B/L	30.5	94	120	80	92	146	50	No	No	No
143	1329505	JS	M	51	R	27.2	89	110	70	99	121	41	No	No	No
144	1314608	GS	M	50	R	23.1	86	160	90	70	129	52	Yes	Yes	No
145	1126249	BH	F	35	L	26.2	76	120	80	142	90	53	No	Yes	No
146	1366346	MB	M	58	B/L	32.7	103	120	80	199	146	41	No	Yes	No
147	1358702	MR	M	68	R	33.2	104	128	80	200	110	45	No	Yes	No
148	1367646	IS	M	40	R	32.1	100	110	80	70	190	50	No	No	No
149	1315430	BS	M	38	R	31.2	110	100	80	90	147	44	No	No	No
150	1314704	R	M	25	L	18.4	80	110	70	60	110	76	No	No	No
151	1071512	R	F	30	B/L	20.1	66	120	80	90	120	50	No	No	No
152	1315777	SK	M	46	VESICAL	20.6	86	140	90	60	100	52	Yes	No	No
153	187030	KU	F	43	R	20.1	74	130	80	99	101	60	No	No	No
154	1304206	RJ	M	50	R	19.5	84	120	80	110	160	42	No	Yes	No
155	1316812	SJ	M	32	B/L	20.1	82	120	80	70	139	36	No	No	No
156	1292063	AKS	M	33	R	28.3	96	130	90	86	129	56	No	No	No
157	1314552	DS	M	19	R	23.6	85	100	70	70	136	76	No	No	No

158	1321548	IS	M	29	L	27.6	96	120	70	90	120	60	No	No	No
159	1320477	MS	M	33	B/L	25.6	85	120	80	94	130	49	No	No	No
160	1325231	NK	F	60	R	19.5	64	160	100	99	161	39	Yes	Yes	No
161	835736	RS	M	45	R	18.6	79	110	90	80	130	56	No	No	No
162	1313525	MS	M	57	L	16.6	56	120	80	196	156	52	No	Yes	No
163	1321699	GJ	M	47	B/L	20.1	91	110	80	80	106	41	No	No	No
164	166811	SS	M	70	R	21.1	88	110	70	97	196	56	No	No	Yes
165	1325540	MS	F	49	R	22.9	60	140	78	184	140	43	No	Yes	No
166	1320244	SG	M	53	VESICAL	27.6	89	120	80	136	199	41	No	Yes	Yes
167	1324598	MK	F	60	L	30.5	78	170	100	142	212	51	Yes	Yes	No
168	1295404	SR	F	61	R	31.3	110	100	60	164	147	66	No	Yes	No
169	1331698	SS	M	50	L	26.3	99	120	80	96	132	54	No	No	No
170	1308190	HSD	M	55	L	27.7	89	130	70	90	120	54	No	No	No
171	1215983	RG	M	52	R	21.1	90	110	80	98	166	41	No	No	No
172	920940	BK	F	57	B/L	20.6	74	138	80	132	96	41	Yes	Yes	No
173	1337063	BG	M	49	R	20.7	84	110	70	80	176	46	No	No	Yes
174	1336981	DD	M	64	R	28.2	96	120	70	80	120	53	No	No	No
175	1295404	SR	F	61	R	19.6	69	156	86	109	110	61	No	Yes	No
176	1339055	GP	M	36	R	20.8	84	100	60	80	142	49	No	No	No
177	1342082	BS	M	36	R	23.4	89	110	70	78	126	60	No	No	No
178	370849	AK	M	25	R	26.2	84	120	80	90	140	66	No	No	No
179	1344416	PS	M	45	B/L	22.9	89	120	80	94	210	41	No	No	Yes
180	1327061	GT	M	32	R	27.8	84	126	80	76	130	57	No	No	No

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The Principal,
DMC, Ludhiana.

Subject: **Approval of Plan of Thesis.**

This is to inform you that the Faculty of Medical Sciences in its meeting held on 29.10.2021 has approved the plan of thesis of **Naman Singhal**, a student of your college for **MCh Urology** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis

A study to evaluate the association between urolithiasis and metabolic syndrome.

Supervisor

Dr. Sandeep Sharma
Prof. & Head,
Dept. of Urology,
DMCH, Ludhiana.

Co-Supervisor

Dr. Arvind Goyal
Assoc. Prof.,
Dept. of Urology,
DMCH, Ludhiana.

Dr. Naveen Mittal
Prof.,
Dept. of Endocrinology,
DMCH, Ludhiana.

The student has to submit the four copies of thesis (along with PDF format) , to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She must directed to attach a photocopy of this letter with the forwarding letter while submitting thesis to the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic,(if any).

Dr. S P Singh MS(Oph)
Controller of Examinations

Note :

183. If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.

184. The student may submit the thesis as per the schedule already conveyed i.e for May/June examination 30th Nov of the preceding the year of examination and for Nov/Dec examinations 31st May of the year of examination.

A STUDY TO EVALUATE THE ASSOCIATION BETWEEN UROLITHIASIS AND METABOLIC SYNDROME

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED

IN PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

MCh

IN

UROLOGY

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES
FARIDKOT

AUGUST, 2021

DR. NAMAN SINGHAL

DEPARTMENT OF UROLOGY
DAYANAND MEDICAL COLLEGE &HOSPITAL
LUDHIANA

ABSTRACT OF PLAN OF THESIS

Title	A STUDY TO EVALUATE THE ASSOCIATION OF UROLITHIASIS AND METABOLIC SYNDROME
For the degree of	MCh Urology
Name of the candidate	Dr.Naman Singhal
Supervisor	Dr Sandeep Sharma, Professor & Head, Department of Urology, DMCH
Co-supervisor	Dr Arvind Goyal, Associate Professor, Department of Urology, DMCH
Co-supervisor	Dr Naveen Mittal, Professor, Department of Endocrinology, DMCH
Institution	Dayanand Medical College & Hospital, Ludhiana
University	Baba Farid University of Health Sciences, Faridkot

Introduction: Urinary stone disease is a common urological disease. Nephrolithiasis continues to be a major cause of morbidity and healthcare spending. Patients with metabolic syndrome have an increased risk of developing nephrolithiasis .The common calculus are calcium oxalate stones, calcium phosphate stones, uric acid stones, calcium magnesium ammonium phosphate stone (triple phosphate stone or struvite stone) and cystine stone .

Aim of Study: 1. To evaluate the relationship of Urolithiasis with metabolic syndrome constituents.

2. To evaluate the biochemical component of stone in metabolic syndrome.

Materials & Methods: The study will be conducted among the patients admitted to Department of Urology, Dayanand Medical College and Hospital, Ludhiana from 1st August 2021. The study design is a Cross-sectional study. Information shall be collected through a pre- designed performa for each patient chosen to be a part of the study with detailed history, clinical examination and complete investigational workup. Details of the study will be explained to each case. Analysis will be done with the collected details. A pre-informed consent from each patient shall be taken.

Clinical Significance: Nephrolithiasis is a common disorder affecting the urinary tract. The morbidity produced by nephrolithiasis to the patients and the huge amount spend on the diagnosis, treatment and follow up leads to search for preventive strategies of nephrolithiasis .Primary and secondary prevention methods therefore tend to revolve mainly around lifestyle improvements, including dietary and other preventive measures.

Keywords: Nephrolithiasis, Metabolic syndrome, Obesity, Calcium, Uric acid

(Signature)	(Signature)	(Signature)	(Signature)	(Signature)
Candidate	Co-supervisor	Co-supervisor	Supervisor	Principal

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"A STUDY TO EVALUATE THE ASSOCIATION OF UROLITHIASIS AND METABOLIC SYNDROME"** exist in the Department of Urology, DMC&H, Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis is genuine and is collected by the candidate himself/herself under our supervision and guidance.

Supervisor

Dr Sandeep Sharma
Professor and Head
Department of Urology
DMCH, Ludhiana

Co-Supervisor(s)

Dr Arvind Goyal
Associate Professor
Department of Urology
DMCH, Ludhiana

Dr Naveen Mittal
Professor
Department of Endocrinology
DMCH, Ludhiana

Head of the Department

Dr. Sandeep Sharma
Professor & Head
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DMCH, Ludhiana

Place : LUDHIANA

Date : 3/9/14

APPROVAL PROFORMA
BY RESEARCH & ETHICAL COMMITTEE
DAYANAND MEDICAL COLLEGE & HOSPITAL, LUDHIANA

Name of candidate	Dr Naman Singhal
Department	MCh Urology
Topic of Thesis	A STUDY TO EVALUATE THE ASSOCIATION BETWEEN UROLITHIASIS AND METABOLIC SYNDROME
Likely date of appearing in PG examination	May/June, 2023
Date of enrollment	31.12.2020
Name of Head of Department	Dr Sandeep Sharma
1) Supervisor **2) Co-Supervisor(s)**	Dr Sandeep Sharma Dr Arvind Goyal Dr Naveen Mittal
Signature of Members of Research Committee with Stamp	**Signature of Members of Ethics Committee with Stamp**
Dr. Harpreet Kaur (Professor & Head, Pathology)	Mr. R K Sharma (Legal Expert)
Dr. Jaspal Singh (Professor & Head, Surgery)	Dr. Ramit Mahajan (Associate Professor, Gastroenterology)
Dr. Dinesh Gupta (Professor & Head, Medicine)	Dr. Anu Sharma (Professor, Anatomy)
Dr. Sandeep Kaushal (Dean Academics & Professor & Head, Pharmacology)	Dr. Sandeep Kaushal (Dean Academics & Professor & Head, Pharmacology)
Dr. Gurpreet S Wander (Vice Principal)	Dr. Gurpreet S Wander (Vice Principal & Professor & Head, Cardiology)
	Dr. Gagandeep Singh (Secretary, Ethics Committee Professor & Head, Neurology)

Approved: Yes / No

Dr. Sandeep Puri
Chairperson
Research Committee
Chairperson
Research Committee

Approved: Yes / ~~No~~

Prof. Arvind Malhotra
Chairperson
Ethics Committee
Chairperson
Ethics Committee

BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT

PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

1	NAME OF THE CANDIDATE AND ADDRESS	DR. NAMAN SINGHAL 4/115A-2 Civil Lines, Church road, Agra-282002, U.P.
2	NAME OF THE INSTITUTE	DAYANAND MEDICAL COLLEGE AND HOSPITAL, LUDHIANA
3	COURSE OF STUDY AND SUBJECT	M.Ch UROLOGY
4	DATE OF ADMISSION OF COURSE	31st December 2020.
5	TITLE OF THE TOPIC	A STUDY TO EVALUATE THE ASSOCIATION BETWEEN UROLITHIASIS AND METABOLIC SYNDROME

6. BRIEF RESUME OF THE INTENDED WORK

6.1NEED FOR THE STUDY

Urolithiasis is one of the most common urological disorder with a significant burden worldwide with a prevalence of around 5%–10% and more commonly reported in men than women.[1] Urolithiasis is also common in India and is often complicated with comorbidities. Metabolic syndrome is a general metabolic condition commonly seen worldwide and has been reported to be increasing in last few decades. It is a group or combination of central obesity, hyperglycemia, dyslipidemia, and hypertension and hence has an increased risk of cardiovascular disease.[2]

It has been known that obesity is a contributing factor for the development of urolithiasis. There has been a significant association between urolithiasis and metabolic syndrome.[3]

The link between urolithiasis and metabolic syndrome has suggested a possible role of multiple metabolic risk factors in the development of urolithiasis.[3,5] The key parameters depicting metabolic syndrome include overweight, arterial hypertension and disturbances of the carbohydrate metabolism.[4]

The New International Diabetes Federation (IDF) requires [6]

Central obesity defined as waist circumference ≥90 cm in men and ≥80 cm in women for Asians, except for Japanese) plus two of the following four factors:

1.Raised Triglycerides ≥150 mg/dl (1.7mmol/L) or specific treatment for this lipid abnormality

2. Reduced HDL cholesterol <40 mg/dl (1.03mmol/l) in males and <50 mg/dl (1.29 mmol/L) in women or specific treatment for this lipid abnormality

3. Raised Fasting plasma glucose ≥100 mg/dl (5.6mmol/L) or previously diagnosed with type 2 diabetes

4. Raised Blood pressure (Systolic BP ≥130 or diastolic ≥ 85 mmHg or on treatment for previously diagnosed hypertension

Nephrolithiasis are polycrystalline aggregates containing various proportions of crystal and organic matrix components. The common

nephrolithiasis calculus are calcium oxalate stones, calcium phosphate stones,uric acid stones,calcium magnesium ammonium phosphate stone (triple phosphate stone or struvite stone) and cystine stone.

Due to advances in the investigation modalities for the diagnosis of nephrolithiasis, stone disease was increasingly diagnosed prior to their symptomatic presentation. And also due to marked advancement in technology, nephrolithiasis was increasingly treated by non invasive methods like Extra corporial Lithotripsy (ESWL) and by minimal invasive procedures like Per cutaneous nephrolithotomy (PCNL). These procedures treat the nephrolithiasis patients with less morbidity and with good results.[7]

Because of profound morbidity due to the disease and during treatment, loss of renal function with end stage renal disease in some neglectedcases and increased cost of expenditure for diagnosis and treatment, there was shift of focus from treatment to prevention of nephrolithiasis.

Metabolic syndrome[8] is a complex of medical disorders; when they occur together have clinical significance like increased risk of developing cardiovascular disease, cerebrovascular accidents, diabetes mellitus (type two) and atherosclerosis. There are different definitions for defining metabolic syndrome and they all include the main components – obesity or waist circumference, hypertension, hyperlipidemia and hyperglycemia.

The associations of metabolic syndrome with nephrolithiasis were showed by many studies[9] in a defined population. It is shown to be associated with metabolic syndrome patient's urinary constituents like decrease in urinary PH, increased urinary calcium and uric acid excretion and decreased excretion of urinary citrate which is an important inhibitor of nephrolithiasis.

We investigate this association in patient population in our institute with nephrolithiasis and compare with individuals without nephrolithiasis.

6.2 REVIEW OF LITERATURE

PATHOPHYSIOLOGY OF CALCULUS FORMATION

Nephrolithiasis contains large amount of crystalline material (97%-98%) and organic matrix providing the framework for deposition of crystals[10].

Calculus formation starts when

1) There is excess excretion of calculus forming salts and precipitation to form nuclei or crystal.

2) There is decrease in substance that inhibits crystal deposition.

3) There is availability of specific macromolecules needed for calculus formation.

The calculus formation inhibitors present in urine were citrate, glycosaminoglycan like heparin sulfate, magnesium, RNA, acid mucopolysaccharides and urinary glycoproteins like Tamm Horsfall glycoprotein and nephrocalcin. Citrate was an important inhibitor ofnephrolithisis and it acts by

1) It reduces the calcium salts saturation in urine by combining with calcium.

2) Directly prevents calcium oxalate nucleation.

3) It inhibits precipitation and growth of Calcium Oxalate crystals.

4) It enhances Tamm Horsfall glycoprotein's inhibitory effect

These inhibitors allow high concentration of Calcium Oxalate crystals in the state of solution. This point of saturation was called as metastable state. It can be proposed that nephrolithiasis was formed from calcium salts in a metastable urine by heterogeneous nucleation.

Calculus analysis shows it contains crystalline and non crystalline component. This non crystalline component was termed as matrix. In nephrolithiasis the matrix commonly account to 2-3%.[11]

The first evidence of crystal retention has been showed by Randall in1940 as plaques of sub epithelial deposits of calcium crystals in renal papillae. These plaques were called Randall's plaques which act as a nidus for urinary calculus formation.

Nephrolithiasis contains mostly calcium (75%). So it was classified in to calcium containing calculus and non calcium containing calculus[12].

Calcium-Containing calculus

· Calcium oxalate – 60%

· Hydroxyapatite- 20%

· Brushite- 2%

Non Calcium Containing calculus

· Uric acid – 7%

· Struvite – 7%

· Cystine -1%.

The derangements causing nephrolithiasis with calcium were due to hypercalciuria, hyperoxaluria, hyperuricosuria, and hypocitraturia. Cystine calculus was formed due defective absorption of renal cystine. Uric acid calculus was formed in acidic urine and Struvite calculus formed in infective urine where urea splitting organisms like Proteus and Klebsiella cause urine alkalization and calculus formation.

Calcium containing calculus

Hypercalciuria

Hypercalciuria was one of the most frequently detected abnormalities found in persons having calcium containing nephrolithiasis. Increased calcium concentrations in urine causes increased urinary calcium salts saturation and reduced urinary calculus inhibitors like urinary citrate.

Pak et al[13]classified the causes of hypercalciuria into three types

· Absorptive hypercalciuria

· Renal hypercalciuria

· Resorptive hypercalciuria

Absorptive Hypercalciuria -was defined as increased urinary calcium following oral calcium load due to increased intestinal absorption of calcium. It usually occurs in 55% of calculus forming patients. It was classified into type 1- when urinary calcium excretion was high in spite of low calcium diet and type 2- when urinary calcium level becomes normal when patient was placed in calcium restricted diet.

Renal hypercalciuria - Of the reabsorbed 98% of filtered calcium, 70% of the absorption occurs in proximal tubule mostly by paracellular pathway. So impaired renal absorption leads to increased urinary calcium leads to secondary hyperparathyroidism. The exact

cause of renal calcium leak was not found but may be due to renal injuries, structural abnormality or functional defect.

Resorptive Hypercalciuria - It was uncommon and mostly due to primary hyperparathyroidism.

Hyperoxaluria

It was defined when urinary oxalate excretion exceeds 40mg/day. Hyperoxaluria[14]divided into

1) *Primary hyperoxaluria* - when it was caused by genetic defect in the glyoxalate metabolism, where normal metabolism of glyoxalate to glycine does not happen and there is increased oxidative conversion of glyoxalate to oxalate occurs. It leads to increased (>100mgs/day) excretion of urinary oxalates. 2) *Enteric hyperoxaluria* - when it was caused by intestinal malabsorbtive state as in inflammatory bowel disease, celiac sprue, intestinal resection surgeries or in bariatric surgeries done for obesity. It was the most common acquired form of hyperoxaluria. 3) *Dietary hyperoxaluria*- Diets rich[15] in oxalates like nuts, spinach, strawberry, chocolate, broccoli and rhubarb can cause hyperoxaluria.

Hyperuricosuria

It was defined as when uric acid excretion[16] in urine exceeds 600mgs/day. The common causes of hyperuricosuria were increased purine intake in diet, gout, myeloproliferative disorder, lymphoproliferative disorder, multiple myeloma, pernicious anaemia, polycythemia, thalassemia, partial or complete deficiency of enzyme hypoxanthine guanine phosphoribosyltransferase, enzyme phosphoribosylpyrophosphate synthetaseoveractivity and renal hypouricemia.

Hypocitraturia

It was defined as when urinary citrare level was below 320mgs/day.

rine (< 5.5).

Uric acid stones

Uric acid stoneswere caused by three main determinants. They were low urine volume, low PH and hyperuricosuria. Of these low urinary PH

was very important and consistent variable for the formation of uric acid calculus.

Cystine calculus

It was caused by cystinuria[17]which was an inherited autosomal recessive disease caused by disorder in intestinal and renal tubular transport of cystine, ornithine, lysine and arginine.

Struvite calculus

Struvite or magnesium ammonium phosphate calculus was discovered by Swedish geologist and named it as struvite after his mentor H.C.G.Von Struvite. It was formed as a result of urinary infection with urea splitting enzyme urease containing organism such as Proteus. Struvite or triple calculus occurs more commonly in females in the ratio of 2:1 when compared to males.

A study was conducted to assess the correlation between metabolic syndrome and urolithiasis in Indian patients. The mean age of total population was 47.26 years with 60.08% of males. Significantly lower mean height and higher weight were observed in patients with metabolic syndrome. Distribution of patients according to BMI significantly ($P < 0.001$) differed between both groups. Overall, 581 (43.12%) patients were obese (BMI >25). Among patients without metabolic syndrome 39.4% of patients were obese; however, in the metabolic syndrome group, 91.3% of patients were obese ($P < 0.001$). Waist circumference was significantly higher in patients with metabolic syndrome (99.82 cm) than those without metabolic syndrome (83.48 cm) ($P < 0.001$). SBP and DBP, triglyceride levels, and FBS levels were significantly higher in patients with metabolic syndrome than those without metabolic syndrome; however, HDL level were significantly reduced in metabolic syndrome group ($P < 0.001$). These observations suggest that metabolic risk factors are predominantly present in urolithiasis patients with metabolic syndrome. Several studies attributed the increased incidence of uric acid stone formation in the obese population to the production of more acidic urine as compared to nonobese patients.[18]

An increased incidence of urolithiasis of up to 75% has been seen in patients who are overweight or obese.[19] Obesity is associated with impaired carbohydrate tolerance and inappropriate calcium response to glucose ingestion. Another reason could be relationship of obesity with changes in the environment of urine leading to urinary stone formation.A database of patient history, body mass index, and serum and urine chemistry was analyzed for 704 consecutive stone formers (467 first time stone formers and 247 recurrent stone formers). Obesity was defined as body mass index greater than 25 kg/m(2). The effect of obesity on stone risk factors and recurrence were stratified according to stone episodes. Of these, 163 (23.2%) patients who had been followed for more than 36 months (median 54, range 5 to 148) were included in recurrence analysis.

It was found that obesity was significantly associated with stone episodes ($p = 0.043$). Obese stone formers excreted increased amounts of sodium, calcium, uric acid and citrate, while the urinary pH in a 24-hour urine sample was decreased compared to nonobese stone formers ($p < 0.05$, respectively). Stone analysis revealed that uric acid stone was significantly more commonly found in the obese patients ($p = 0.046$). Anoverly acidic urine has been described as a renal manifestation of the metabolic syndrome in patients with kidney stone disease. A study examined the association between the metabolic syndrome and urine pH in individuals without a history of nephrolithiasis where A total of 148 adults who were free of kidney stones were evaluated in outpatient cross-sectional study. Height, weight, BP, fasting blood, and 24-h urine chemistries were obtained. Urine pH was measured by pH electrode. The following features of the metabolic syndrome were evaluated: BP; body mass index; and serum triglyceride, glucose, and HDL cholesterol concentrations. The degree of insulin resistance was assessed by the homeostasis model assessment of insulin resistance. Participants with the metabolic syndrome had a significantly lower 24-h urine pH compared with participants without the metabolic syndrome.[20]

Another study also reported incidence of diabetes in urolithiasis patients with metabolic syndrome. Insulin resistance has been correlated to the reduction in renal ammonium production and low urinary pH, resulting into formation of urolithiasis.[21] Moreover, direct correlation between low urinary pH and number of metabolic syndrome risk factors as well as inverse correlation between degree of insulin resistance and urinary pH have been shown in a crosssectional study performed by Maalouf et al. Various recent studies reported the varying percentage of patients with metabolic syndrome in the range of 11.5%–38.3% with higher prevalence of urolithiasis among them as compared to patients without metabolic syndrome.

It showed that proportion of patients with hyperuricemia were significantly higher in metabolic syndrome group than in nonmetabolic syndrome group. These observations are parallel to the study by Strohmaier et al. who reported hyperuricemia in 37% of patients with urolithiasis.[22]

As discussed earlier, number of metabolic components responsible for metabolic syndrome affects severity of renal stone disease. In addition to obesity, other metabolic disorders like diabetes mellitus, hypertension and dyslipidemia also play a role in increased severity of kidney stone disease. Kohjimoto et al. observed 1.8 times larger odds of recurrent formation of stones as well as the formation of multiple stones in patients with four metabolic traits compared to those with zero traits.[23]

As the number of metabolic components increased, a significant increasing trend in mean waist circumference, triglycerides, FBS, SBP, and DBP ($P < 0.001$) and a significant decreasing trend in mean HDL ($P < 0.001$) were observed in urolithiasis patients with metabolic syndrome. It showed that female patients were 19.6 times (1/0.051) more likely to develop metabolic syndrome than male patients ($P < 0.001$). This might be due to the high prevalence of cardiometabolic risk factors such as hypertension, increased waist circumference, concomitant increases in hypertriglyceridemia and fasting glucose in females.[24]

Furthermore, hormonal regulation of body weight and adiposity in females could contribute to the high risk of metabolic syndrome. A metaanalysis by Kuk and Ardern suggested that abdominal obesity was the dominant feature of metabolic syndrome in women.[24]

It has been reported that rise in metabolic components (such as increasing waist circumference, triglycerides, FBS, blood pressure) was directly associated with increased risk of metabolic syndrome in patients diagnosed with urolithiasis($P < 0.05$). However, decreasing HDL was associated with reduction in the likelihood of exhibition of metabolic syndrome in patients with urolithiasis Present study also reported that patients with elevated serum uric acid were 5.68 times more likely to exhibit metabolic syndrome than patients with normal serum uric acid levels ($P = 0.006$). These results indicate the strong association between hyperuricemia and risk of metabolic syndrome in patients with urolithiasis.[25]

6.3 AIMS AND OBJECTIVES OF THE STUDY

- To evaluate the relationship of Urolithiasis with metabolic syndrome constituents.
- To evaluate the biochemical component of stone in metabolic syndrome.

7.0 MATERIALS AND METHODS

Study design - The study design is a Cross-sectional study.

7.1 SOURCE OF DATA:

The study will be conducted among the patients admitted to department of Urology, Dayanand Medical College and Hospital, Ludhiana from 1st August 2021 to 31st January 2023.

7.2 METHOD OF COLLECTION OF DATA

Information shall be collected through a pre- designed performa for each patient chosen to be a part of the study with detailed history, clinical examination and complete investigational workup. Details of the study explained to each case. Analysis will be done with the collected details prospectively. A pre-informed consent from each patient shall be taken.

INCLUSION CRITERIA

1. Age ≥ 18
2. Either gender
3. Patients with unilateral or bilateral Urolithiasis

EXCLUSION CRITERIA

1. Patients with congenital renal abnormalities
2. Chronic renal failure patients
3. Patients with metabolic bone disorder or taking treatment for osteoporosis
4. Patients with major debilitating disease like cancer
5. Pregnancy

METHOD OF COLLECTION OF DATA:

Case admitted in Dmch of Age ≥ 18 and either gender with unilateral or bilateral Urolithiasis consenting to participate in the study and not having any above mentioned exclusion criteria will be included in the study. Demographic data and standard of history and general examination and systemic examination will be collected in structured way.

All individuals will undergo ultrasound evaluation/ NCCTKUB of both kidneys.

All patients will undergo measurement of waist circumference, their systolic and diastolic blood pressure, fasting blood sugar, serum triglycerides and serum HDL cholesterol levels

Measurements will be according to The New International Diabetes Federation (IDF) which requires

Central obesity defined as waist circumference ≥90 cm in men and ≥80 cm in women for Asians, except for Japanese)

plus two of the following four factors:

1.RaisedTriglycerides ≥150 mg/dl (1.7mmol/L) or specific treatment for this lipid abnormality

2.ReducedHDL cholesterol <40 mg/dl (1.03 mmol/L) in males and <50 mg/dl (1.29 mmol/L) in women or specific treatment for this lipid abnormality

3. Raised Fasting plasma glucose ≥100 mg/dl (5.6 mmol/L) or previously diagnosed with type 2 diabetes

4.Raised Blood pressure (Systolic BP ≥130 or diastolic ≥ 85 mmHg or on treatment for previously diagnosed hypertension

Ultrasonogram /NCCTKUB

All patients including all cases will undergo ultrasonogram/NCCTKUB

Waist circumference

Waist circumference will be measured using a non stretchable measuring plastic tape. The measurement will be taken with the individuals in a relaxed and standing position with both feet together. Waist circumference measured at midpoint of lowermost border of twelfth rib and upper border of iliac crest at the end of expiration.

Measurement of Blood Pressure

Systolic and diastolic BP will be measured using sphygmomanometer. Blood pressure will be obtained with the individuals in calm and sitting position. Two readings will be taken with five minutes apart and their average will be taken into consideration.

Stone Analysis

After surgery stone sample will be send for stone analysis for composition of stone

SAMPLE SIZE – Time bound study

DURATION OF STUDY – 1st August 2021 to 31st January 2023

OUTCOME- The outcome of the study will be defined as increase risk of stone formation in patient with metabolic syndrome and its constituent and common composition of stone in the patient with metabolic syndrome.

STATISTICAL ANALYSIS

Data will be described in terms of range, mean ±, standard deviation, frequencies (number of cases) and relative frequencies (percentages)

For discrete data -proportion is computed and the mean and standard deviation will be computed for the continuous data. The chi square test will be applied to compare the proportions between the groups to assess the statistical significance. All analyses will be two tailed and p <0.05 will be considered significant. SPSS version 21.0 will be used for data analysis.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

Routine, Renal Ultrasound, NCCT – KUB, Urinary stone Biochemical profile

7.4 HAS ETHICAL CLEARENCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Attached here with.

8.0 LIST OF REFERENCES

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PROFORMA

Sr. No. ___

NAME : **AGE/SEX :**

M.R.D.NO: **Adm. NO :**

DOA : **DOD :**

ADDRESS :

History of Present illness :

Past History :

Family History :

Other Comorbidities :

DM

HTN

Drug therapy

Previous Treatment / Surgery / Intervention biopsy :

Signature of Candidate **Signature of Supervisor**

General Physical Examination :

Apperance –

BP PR RR TEMP

SYSTOLIC BP

DIASTOLIC BP

WAIST CIRCUMFERENCE -

Height

Weight

BMI

Significant Systemic Examination :

Chest -

Per – Abdomen -

CVS -

CNS –

Signature of Candidate

Signature of Supervisor

Investigations **Date- (__/__/____)**

Hb	
Tlc	
PT/INR	
S.Creatinine	
Urea	
S.Triglycerides	
HDL	
Fasting Blood Sugar	

USG KUB, Date- (__/__/____)

NCCT- KUB, Date- (__/__/____)

URINE ROUTINE Date- (__/__/____)

PHYSICAL EXAMINATION	CHEMICAL EXAMINATION	MICROSCOPIC EXAMINATION
QUANTITY	Ph	EPITHELIAL CELLS
COLOUR	PRO	PUS CELLS
DEPOSITS	GLU	R.B.C.s
SG	NITRATE	CRYSTALS
		CASTS
		YEAST
		BACTERIA

Type of Surgery performed – Date- (__/__/____)

Stone Analysis Report - Date- (__/__/____)

Dams

Signature of Candidate **Signature of Supervisor**

INFORMED PATIENT CONSENT

Date: _____

I.....D/o, W/o, S/o.....
.....am willing to participate in the study **"A STUDY TO EVALUATE THE ASSOCIATION BETWEEN UROLITHIASIS AND METABOLIC SYNDROME"** The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason.

....
Signature of the Witness Signature of the patient

Name:

Signature of Candidate **Signature of Supervisor**

मरीज अनुमति फार्म

तिथि _____

मैं _____ पत्नी/पुत्र/पुत्री _____

निवासी _____

इस शोधकार्य "A STUDY TO EVALUATE THE ASSOCIATION BETWEEN UROLITHIASIS AND METABOLIC SYNDROME" में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

_____

गवाह के हस्ताक्षर

नाम:

_____

रोगी के हस्ताक्षर/अंगूठे का निशान

नाम:

_____

अन्वेषक केहस्ताक्षर

_____

विद्यार्थी के हस्ताक्षर

ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ _____

"A STUDY TO EVALUATE THE ASSOCIATION BETWEEN UROLITHIASIS AND METABOLIC SYNDROME" ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ। ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

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ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____ ਮਿਤੀ_____

ਪਤਾ _____ ਪਤਾ _____

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ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

Pawy

ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ